Child influenza vaccination
the importance of parental perception of side-effects

Smith, Louise Elizabeth

Awarding institution:
King's College London

Child influenza vaccination: the importance of parental perception of side-effects

Louise Elizabeth Smith

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Department of Psychological Medicine

Institute of Psychiatry, Psychology and Neuroscience

King's College London

Abstract

Influenza is a major cause of death worldwide. In an attempt to decrease the morbidity and mortality associated with influenza, as well as its financial cost and burden to healthcare services, the influenza vaccine has been offered to children in England since 2013. However, uptake is low. Fear of side-effects has been well-established as one of the major factors contributing to vaccination refusal. But not all side-effects perceived after vaccination can be attributed to the vaccine. Multiple psychological factors related to the 'nocebo' effect may influence parental perception of side-effects from vaccination. The role of cognitive biases and heuristics in vaccination has been well-explored. However, there is no research investigating whether information processing biases are associated with vaccination behaviours. In this thesis, I aimed to identify psychological factors which were associated with uptake of the child influenza vaccine and parental perception of side-effects from vaccination.

I conducted a nationally-representative online survey of parents of vaccine-eligible children in the 2015/16 influenza season (n=1001). Results suggested that believing that the vaccine caused adverse effects were associated with not vaccinating one's child and perceiving side-effects from vaccination in those who did vaccinate. However, the cross-sectional nature of this study made it difficult to infer causality. To better investigate predictors of parental perception of side-effects from vaccination I conducted a prospective cohort study in the 2016/17 influenza season (n=270); the last follow-up was at the end of the 2017/18 influenza season (n=232). I found that multiple psychological factors were associated with parental perception of side-effects from vaccination. In particular, pre-vaccination expectations were strongly associated with perceiving side-effects from vaccination. I also investigated rates of re-vaccination for influenza in the 2017/18 season and factors associated with re-vaccination. Results indicated that over one in six children were not re-vaccinated for influenza in 2017/18. Perceived severity of side-effects from vaccination in 2016/17, and parental worry about side-effects perceived, were associated with not re-vaccinating one's child in the 2017/18 season.

While many studies have identified that parental perception of side-effects plays a major role in vaccination refusal, few studies have investigated potential causes of parental perception of symptoms. My results indicate that managing parents' expectations about the incidence and severity of vaccine side-effects may decrease parental perception of

side-effects from vaccination. Decreasing worry about side-effects perceived may increase vaccine uptake and re-vaccination rates. These are novel targets for vaccine communications and interventions.

Publications from thesis

1. Smith LE, Amlôt R, Weinman J, Yiend J, Rubin GJ. A systematic review of factors affecting vaccine uptake in young children. Vaccine. 2017;35(45):6059-69. (Chapter 2)
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3. Smith LE, Webster RK, Weinman J, Amlôt R, Yiend J, Rubin GJ. Psychological factors associated with uptake of the childhood influenza vaccine and perception of post-vaccination side-effects: A cross-sectional survey in England. Vaccine. 2017;35(15):1936-45. (Chapter 5)
4. Smith LE, Weinman J, Amlot R, Yiend J, Rubin GJ. Parental expectation of side effects following vaccination is self-fulfilling: a prospective cohort study. Ann Behav Med. 2018. (Chapter 6)
5. Smith LE, Amlot R, Weinman J, Yiend J, Rubin GJ. Why do parents not re-vaccinate their child for influenza? A prospective cohort study. Under review. Ann Behav Med. (Chapter 6)

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Abbreviations

aOR	adjusted odds ratio
ADHD	attention-deficit hyperactivity disorder
ANOVA	analysis of variance
CI	confidence interval
GP	general practice
HCW	healthcare worker
HIV	human immunodeficiency virus
HPV	human papillomavirus vaccine
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
JCVI	Joint Committee on Vaccination and Immunisation
LAIV	live attenuated influenza vaccine
MeSH	medical subject heading
MMR	measles, mumps and rubella
NHS	national health service
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SPSS	Statistical Package for the Social Sciences
UK	United Kingdom
USA	United States of America
UTD	up-to-date
WHO	World Health Organization

Chapter 1. Influenza and the child influenza vaccine

What are the deadliest diseases? When asked, many will point to infectious diseases currently attracting the greatest media attention, such as the Ebola and Zika viruses. Others might consider diseases that perpetually plague the developing world and result in periodic charity appeals in the West, for example cholera or malaria. People would rarely include common seasonal influenza on their list of the most troubling infectious diseases. Yet seasonal influenza causes up to 650,000 deaths a year (1); a great many more than diseases which often attract considerably more attention. For example, the Ebola outbreak in West Africa caused 11,310 deaths between December 2013 and June 2016 (2). The latest figures indicate that there have been 303 deaths (of which 255 are confirmed and forty-eight are probable) in the Ebola outbreak declared on 1st August 2018 (3). The Zika virus has been detected in 86 countries and has caused multiple outbreaks. One of the countries most affected by the Zika virus is Brazil, with over 241,000 cases identified since 2016 (4, 5). However, Zika virus causes severe neurological complications in new-borns rather than death (6). Other diseases which attract a huge amount in charity donations also cause fewer deaths per year. For example, influenza causes almost seven times more deaths annually than cholera (estimated at 95,000) (7) and 50% more deaths annually than malaria (445,000 in 2015 and 445,000 in 2016) (8). Annual estimates of deaths for influenza also surpass the number of deaths for one of the most common forms of cancer: breast cancer (627,000 in 2018) (9). This stark fact has led to a raft of measures being introduced by governments around the world to combat influenza. One of them, child vaccination, has great potential. Improving the uptake of the child influenza vaccine, and saving lives, is the aim of this thesis. But before we consider how to do that, we must first understand the basics. What is influenza? How well does vaccination work? And, most importantly, why would people choose not to vaccinate their child?

Influenza is a common viral illness which causes symptoms such as a high temperature, headache, coughing, aches and pains and a blocked or runny nose (10). There is no single 'influenza virus.' Rather, different strains of virus circulate at the same time, with some strains becoming more dominant and others less dominant over time. There are three modes of transmission for influenza; contact transmission (direct and indirect), droplet transmission and airborne transmission (11, 12). Contact transmission occurs

when a susceptible host touches an infected individual (direct) or an intermediate contaminated object (indirect). Droplet transmission occurs when an infected individual coughs, sneezes or speaks, releasing droplets from the respiratory tract into the air. These droplets then come into contact with the nasal or oral mucosa of a susceptible host. Airborne transmission occurs when droplet nuclei are suspended in the air by aerosolisation and inhaled by susceptible hosts. While for most people who contract influenza, symptoms will resolve within a week, for others in 'at risk' groups such as young children, the elderly and those with existing medical conditions, influenza can cause major complications (13). In the worst cases, influenza can kill.

Estimates of the incidence of influenza and the number who die from it are difficult to provide because laboratory confirmation of influenza is not sought in routine general practice (14). Other illnesses also produce influenza-like symptoms; patients who display such symptoms in the absence of laboratory confirmation tend to be diagnosed with influenza-like illness (ILI). Annually, it is estimated that there are 779,000 general practice (GP) consultations, 19,000 hospital admissions and 10,500 deaths from influenza A and B in England and Wales alone (14). When including secondary bacterial infections and deaths from circulatory disease and other causes which are attributable to influenza, the number of estimated annual deaths rises to 24,800 (14). Evidence shows that 16,415 excess deaths (above the 'baseline' usually expected) were registered in the United Kingdom (UK) over the 2014/15 influenza season (15). While not the sole cause, a large number of these deaths were attributable to influenza (16). Worldwide, seasonal influenza epidemics may cause up to five million cases of severe illness and 650,000 deaths a year, with children being among those with the highest risk of complications (1).

Influenza is a great burden to healthcare services in the winter months, having knock-on effects for other care provided by hospitals. For example, during the 2017/18 influenza season, National Health Service (NHS) trusts were told by NHS England to defer all non-urgent in-patient elective care from 21st December 2017 (17) to the 31st January 2018 (18). This was in part due to the 'sustained pressure over the Christmas period with high levels of respiratory illness' (18).

In addition to the morbidity and mortality associated with influenza and the burden to healthcare services, the financial cost can also be considerable. Whilst the economic cost of influenza is poorly researched in the UK, one study indicated that the cost of general practice visits and hospital admissions in low-risk patients who are not

vaccinated is approximately £111,529,226 more per year than in those who are vaccinated (19). This number is likely to be an underestimate, as it does not take into account the cost of influenza which may have been contracted in hospitals, nor does it include costs such as absence from work, loss of productivity, and the potential cost of childcare should a child or their parent be taken ill. In Western Europe, paediatric influenza caused children to be absent from day care or school for between 2.8 and 12 days and their parents to be absent from work for between 1.3 to 6.3 days per influenza episode (20). Differing influenza severity and location of recruitment of the child (e.g. emergency department, physician's office, or the community) caused the variation in estimates. Child vaccination is a cost saving intervention (21, 22). Vaccinating all children, rather than only 'at risk' children, is also cost-effective, with savings being more pronounced when vaccinating younger children (23). Further studies are needed to give a better understanding of the true financial cost of influenza and savings attributable to vaccination in the UK.

The burden of influenza in children is significant. For example, estimates indicate that up to 9.8% of children aged zero to fourteen years present to their primary care practice with influenza in an average season (24). The burden of influenza seems to be greater in young children, with children aged five and under having more severe outcomes than older children and adults (25). The rate of general practice consultations for influenza-like illness is higher in children aged four and under compared to those aged five to fourteen (24). Hospitalisation associated with influenza is also greater in younger children, ranging between 104 per 10,000 in children under six months and 4 per 10,000 in children aged five to fourteen (26). Children are also good transmitters of influenza (27, 28), dubbed 'super-spreaders' (29) due to their less than optimal hand and respiratory hygiene, high number of people they are in contact with every day and their increased physical contact with others (30, 31). So seriously is the ability of children to spread influenza amongst themselves and their community taken, that school closures are commonly discussed as a key strategy for limiting the spread of influenza during a pandemic (32).

Vaccination is one of the most effective ways of preventing influenza (33). In the UK, yearly influenza vaccination is offered to groups that are most vulnerable to complications from influenza, including pregnant women, older adults and people with underlying medical problems (34). In 2012, the British Joint Committee on Vaccination and Immunisation (JCVI) recommended that the influenza vaccination programme be

extended to include children aged two to sixteen, a process that began in September 2013 (35). The child influenza vaccine was implemented in the UK, being offered for free, to limit the number of children who suffer from complications of influenza, prevent the spread of influenza and reduce morbidity and mortality among adults who may contract influenza from children.

Other countries including the United States of America (USA) (36), Canada (37), Estonia, Poland, Austria, Finland, Latvia, Slovenia, Malta and Slovakia (38) also recommend annual child vaccination for influenza, although differences exist in the age groups and vaccines that are recommended. In the UK it is predicted that with 50% vaccine uptake in two to eighteen year olds and vaccine efficacy of 80%, up to 5.3 million influenza infections per year could be averted; with 2.3 million infections prevented in children aged two to eighteen, and 3 million infections prevented through herd immunity in other age groups (39). Vaccination could also cause substantial reductions in clinical burden, potentially averting 700,000 general practice consultations, 19,200 hospitalisations and 14,740 deaths annually (39).

Children between the age of two and sixteen in the UK are vaccinated using the Fluenz Tetra live attenuated influenza vaccine (LAIV); a nasal spray. This is a different vaccine from the inactivated injected vaccines commonly used in adults, and was chosen due to its increased efficacy in children (40). Fluenz Tetra is contraindicated for children who have an egg allergy. In addition, because the vaccine contains porcine gelatine there is some controversy in the Muslim community as to whether or not the vaccine should be accepted (41). In cases where LAIV cannot be given to children, the injected vaccine may be administered as an alternative (27). Although the patient information leaflet (PIL) for the vaccine states that each child should receive two doses of LAIV, the JCVI has recommended that children only receive one dose, due to the small additional protective value of the second dose (35). Vaccination for influenza is recommended yearly due to the constant mutation of the influenza virus and protects an individual for approximately six to eight months (42).

Each year, influenza vaccines protect people from three or four different influenza strains (trivalent or quadrivalent vaccines respectively). Fluenz Tetra was trivalent in the 2013/14 season but has been quadrivalent since the 2014/15 season (43). Strains to be included in influenza vaccinations are recommended by the World Health Organization (WHO) twice a year; once for vaccination in the Northern hemisphere and once for vaccination in the Southern hemisphere (44). Identification of strains is based on those

that have been circulating prominently in the opposite hemisphere in the previous winter period. For example, in the UK the winter period lasts from October to May (45), whereas in Australasia, most people contract influenza between May and September (46). This imprecise method of choosing vaccination strains can lead to a mismatch in the strains of influenza circulating and those included in vaccinations, decreasing a vaccine's effectiveness.

Vaccine effectiveness refers to the 'real world' proportion of cases that are avoided in those vaccinated compared to those not vaccinated, while vaccine efficacy refers to the proportion of cases avoided in tightly controlled conditions (47). It is estimated that the incidence of laboratory-confirmed influenza can be reduced by 8.2% to 5.9% with a well-matched vaccine, preventing 1.2 million cases of influenza in England; 73% of this protective effect is due to indirect protection or herd immunity (48). There is some evidence that influenza vaccines which have only 10% efficacy could still significantly reduce morbidity and mortality, even beyond those age groups which are vaccinated (49). For example, even if a vaccine is not well-matched, vaccination could still prevent up to 400,000 cases of influenza, 56% of which through indirect protection (48).

1.1 Uptake of the vaccine in England

The child influenza vaccine programme is implemented differently across countries within the UK (50). In England, the vaccine was offered to all two to three year-olds through their general practice and piloted in primary-school age children in its first year (2013/14 influenza season) (51). Since then, the vaccine has been offered to increasingly older children each year (see Table 1) (52, 53). Routine vaccination in schools (school year one and two) started in the 2015/16 influenza season (54). In the 2017/18 influenza season, children aged four started to be vaccinated through their school (school year reception) rather than at their general practice (55).

To date, uptake in children aged two to four in England has consistently been around 30% to 40% (15, 56-58), while uptake in primary school-aged children is slightly higher, at 53% to 58% (57, 58). Uptake in the 2017/18 influenza season was somewhat higher than previous years (59). A full breakdown of national uptake figures is shown in Table 1. There are no data available indicating the proportion of vaccinated children who are re-vaccinated for influenza the following year.

Table 1. Percentage of children vaccinated with the child influenza vaccine across ages and influenza seasons in England

Age in years	2	3	4	4 to 5 (School Reception)	5 to 6 (School Year 1)	6 to 7 (School Year 2)	7-8 (School Year 3)	8-9 (School Year 4)
2013/14 (56)	42.6	39.5	N/A		N/A	N/A	N/A	N/A
2014/15 (15)	38.5	41.3	32.9		N/A	N/A	N/A	N/A
2015/16 (57)	35.4	37.7	30.0		54.4	52.9	N/A	N/A
2016/17 (58)	38.9	41.5	33.9		57.6	55.4	53.3	N/A
2017/18 (59)	42.8	44.2	N/A	62.2	61.0	60.4	57.6	55.8

Uptake of the influenza vaccine is notably worse than many other routine child vaccinations, for which uptake tends to be around 90-95% (60, 61). Uptake rates fell short of targets set by Public Health England (PHE) in the 2015/16 and 2016/17 influenza seasons; targets which were themselves already modest (40% vaccination in those aged two to four) (50, 52). Among all groups for whom the influenza vaccine is recommended, children vaccinated at their primary care practice have the lowest uptake rate (62).

Child influenza vaccination has become an increasing priority for Public Health England, NHS England and the Department of Health, with the 'Stay Well This Winter' campaign emphasising the child influenza vaccine (63). Statements highlighted that the 'children's nasal spray flu vaccine plays an important role in protecting children, [one's] families and others in the community from flu during the winter' (64). Other messages mentioned the 'quick, effective and painless' nature of the vaccine (63), that 'young children's bodies can find it hard to cope with flu,' and that the 'vaccine helps to reduce the spread of flu to other more vulnerable family members' (65). In September 2017, Public Health England and the NHS brought out an advert for the child influenza vaccine (66) which is shown on national television.

Despite low uptake rates since its introduction to the vaccine schedule, the child influenza vaccine has been shown to limit the spread of, and decrease the cost associated with, seasonal influenza (67). Piloting of the child influenza vaccine in primary school children in the 2014/15 influenza season (in which uptake was 56.8%)

was shown to decrease general practice consultations for influenza-like illness by 94% and hospital admissions for influenza by 93% in children aged five to ten (68). The positive effects of vaccinating primary school children were also felt outside the vaccinated age group. In pilot areas, the number of general practice consultations for influenza-like illness decreased in over-seventeens (59% reduction) and under-fives (92%, p=.052) (68).

Since its introduction to the vaccine schedule in the UK, the child influenza vaccine has had varying levels of effectiveness. In the 2015/16 influenza season, the vaccine was effective in reducing hospitalisation for laboratory-confirmed influenza, with a vaccine effectiveness of 54.5% (95% CI [31.5% to 68.4%]) in all children eligible for the vaccine (two to six year olds) (69). In the 2016/17 season, vaccine effectiveness was 65.8% (95% CI [30.3% to 83.2%]) for influenza A and B in children aged two to seventeen (70, 71). Overall vaccine effectiveness in the 2017/18 influenza season was lower (26.9% (95% CI [-32.6% to 59.7%]), due to the poor effectiveness of the A(H3N2) strain included in the vaccine (72).

1.2 Side-effects

As with all vaccines, the child influenza vaccine can cause side-effects. The frequency of side-effects as indicated by the patient information leaflet for Fluenz Tetra are shown in Table 2. Vaccine side-effects are mostly ‘mild in nature and short term’ (73). Data from post-licensure surveillance indicates that on average, side-effects occur on the day of vaccination (74).

Table 2. Side-effects of Fluenz Tetra as described in the patient information leaflet

Very common (may affect more than 1 in 10 people)	**Common** (may affect up to 1 in 10 people)	**Uncommon** (may affect up to 1 in 100 people)	**Very rare** (may affect up to 1 in 1,000,000 people)
Runny or stuffy nose	Fever	Rash	Severe allergic reaction
Reduced appetite	Muscle aches	Nose bleed	
Weakness		Allergic reactions	
Headache			

Although large randomised-controlled trials are routinely conducted before licensing new medications, few trials use a placebo arm. The Declaration of Helsinki (75) states

that where an effective treatment is available for the condition, participants in trials should not be assigned a treatment which is less effective (76). Therefore, many clinical trials use the current best treatment as a control, rather than a placebo group. Where studies using a placebo group do exist, they are particularly informative about the true incidence of adverse effects that are attributable to a medication.

Initial clinical trial data for the quadrivalent vaccine Fluenz Tetra compared it with the trivalent vaccine Fluenz/FluMist in children aged two to seventeen years using a randomised, double-blind study (77). These data indicated that 47.9% children given Fluenz Tetra experienced at least one symptom in the two weeks after vaccination, compared to 47.4% of those vaccinated with Fluenz/FluMist (77). More recently, a randomised, double-blind study in children aged seven to eighteen years compared Fluenz Tetra to placebo (78). In this trial, 41.7% of children vaccinated with Fluenz Tetra reported symptoms in the two weeks following vaccination, compared to 40.6% in the placebo arm (no significant difference); the most common symptoms in both groups were a runny or stuffy nose, cough and sore throat (78). This finding raises important questions about the true causes of the side-effects commonly attributed to the child influenza vaccination. I will return to these later in the thesis. For now, it is sufficient to note that, regardless of their cause, around 40 to 50% of children appear to experience symptoms following vaccination.

Side-effects from vaccination are an important consideration in any discussion about vaccination and may affect child influenza vaccine uptake in two ways. First, fear of side-effects associated with vaccination is often cited by parents as a reason for not initially vaccinating their child. For example, during the 2009/10 influenza pandemic, 50.6% of Dutch parents reported that they did not vaccinate their child for 'fear of side-effects/harmful consequences' (79). Secondly, perceiving side-effects from vaccination might negatively affect parents' decision to re-vaccinate their child for influenza in subsequent years. For example, in one study of parents who vaccinated their child aged six months to seven years for seasonal influenza, 63% of those who perceived side-effects reported being uncertain about, or likely to refuse future influenza vaccinations for their child (80).

Perceiving side-effects from the child influenza vaccine might also negatively influence parents' perceptions about other vaccines and medications. For example, parents may consequently believe that their child is more sensitive to medicines. Parents' perceptions about medicines in general, future treatment decisions for the child and

adherence to medications may also be negatively influenced. This is certainly the case in adults, with those who hold more negative beliefs about medicines showing decreased adherence to medications (81).

1.3 Conclusions

The burden of influenza, in terms of morbidity, mortality, impact on healthcare services and financial cost, is considerable. Vaccination is one of the most effective ways to prevent the spread of influenza, but vaccination uptake remains low, especially in children. Side-effects from the child influenza vaccine are commonly perceived and may negatively affect parents' future vaccination decisions, as well as altering beliefs about medicines and perceptions of how sensitive their child is to medicines. Although there is substantial scope to improve influenza vaccine uptake for children, understanding why uptake is low, and why side-effect perception by parents is high, is an essential first step in this process. To identify factors which might be important in influencing parental influenza vaccination behaviours I conducted two systematic reviews: one investigating psychological, social and contextual factors affecting vaccine uptake in young children, and the second investigating psychological and social factors affecting parental perception of symptoms in their children. These reviews are reported in Chapters 2 and 3.

Chapter 2. Systematic review of factors affecting vaccine uptake in young children

In 2015 almost six million children died globally before the age of five (82). Over half died from preventable infectious diseases (83). Although vaccination is one of the best ways of preventing the spread of disease (84) and reducing morbidity and mortality (85), some parents choose not to vaccinate their child. While in developing countries, lack of access to vaccination and family characteristics such as low education, literacy and socio-economic status present some of the key reasons why children are not vaccinated (86), in developed countries parents often make conscious decisions not to use readily available vaccines. Understanding how to encourage uptake is an important public health aim.

Many studies assessing parental decision making about vaccination are guided by an explicit theory of behaviour change (e.g. (87-89)), which identifies potential factors which may predict vaccination behaviour (90). Vaccine refusal has been associated with: perceived costs and lack of benefits of vaccination, such as believing that vaccines cause short- or long-term side-effects (91) or are ineffective (92); general beliefs, such as believing that children receive too many vaccinations and that vaccines overload the immune system (93); conflict with religious beliefs (94); distrust of healthcare systems and governments (91, 95); and emotional factors such as preferring to suffer the negative consequences of not vaccinating rather than those caused by vaccinating (92). Other commonly cited factors associated with vaccine refusal include forgetting and not knowing that the child needs the vaccine (91, 95).

Parental personal characteristics, such as being unemployed and having a lower socio-economic status (96) are also associated with child vaccine uptake, although the direction of associations in developed countries are unclear. For example, an association has been found between greater education and both vaccine uptake (97) and vaccine refusal (98); the role of age is also unclear (90). Yet while it is important to identify populations with low vaccine uptake to determine target audiences of public health messages or interventions, the identification of demographic factors associated with vaccination is less useful for informing the content of public health communications; here psychological, social and contextual factors become more important.

Moreover, while decisions will undoubtedly be made by parents based on information presented by the media, friends and family as well as factors discussed above, do individuals also have an underlying propensity which affects their vaccination decision? There is ample evidence that factors such as heuristics and cognitive biases affect peoples' judgement when making decisions (99). Heuristics refers to the use of simple judgements rather than complex assessments of probabilities for an outcome to occur (99), while cognitive biases refers to the tendency to systematically choose a particular, often erroneous outcome, rather than the expected outcome, when presented with a certain type of evidence (100, 101). Heuristics and biases are known to exert a significant influence on vaccination behaviour (101, 102). In part, a decision not to vaccinate one's child may reflect the influence of these cognitive processes.

Past literature reviews on factors associated with vaccine uptake have focused on vaccines that have caused controversy in the media, such as combination vaccines including the measles, mumps and rubella vaccine (MMR) (93) and other relatively recently recommended vaccines, such as the human papillomavirus vaccine (HPV) (103). However, the highly charged media-driven debate over such vaccinations makes it difficult to generalise from them to other vaccinations. Identifying the wider barriers to vaccination is important as it allows public health messages to target those variables most consistently associated with non-vaccination.

For this chapter, I conducted a systematic review to identify psychological, social and contextual factors affecting the uptake of routine childhood vaccination for healthy children aged five and under in high-income countries.

2.1 Method

I carried out a review in accordance with PRISMA criteria (104). I searched Embase, Medline, PsycINFO, Maternity and Infant Care, Health Management Information Consortium and Social Policy and Practice through OvidSP, and Scopus. Databases were searched from inception to the 22nd November 2016. I used the following search terms: ((vaccine* OR innocul* OR immunis*) AND (child* OR newborn OR infant OR baby) AND (uptake OR adherence OR compliance OR decision* OR hesitanc* OR concern OR doubt)). Where possible, I limited the search to human studies. A MeSH terms search yielded 52,429 citations. Checking a random sample of 100 of these yielded no relevant papers. The MeSH search was therefore abandoned as impractical. References and forward citations of included articles were also searched.

2.1.1 Inclusion criteria

Inclusion criteria were:

Participants: Studies were included if children were aged five or under. Studies were excluded if children were recruited because of pre-existing ill health.

Predictors/Exposures: Studies were included if they presented data on the association between possible psychological predictors and childhood vaccination or gave a quantitative account of parents' self-reported reasons for or against vaccination. Studies presenting only demographic predictors, predictors related to the mode of delivery of information, or presence or frequency of vaccination appointment reminders were excluded.

Outcomes: Studies were included if they presented data on uptake of a named vaccine and if the vaccine was part of the routine vaccination schedule in that region.

Study reporting: Studies using quantitative methodology which were conducted in high-income countries (as defined by the World Bank (64)) were included. For pragmatic reasons, I included only studies published in English.

2.1.2 Data extraction

For each study, I extracted details concerning country, study design, vaccine, psychological predictors of vaccine uptake and reasons for and against vaccination.

2.1.3 Risk of bias

Risk of bias was assessed using an adaptation of the Downs & Black (105) checklist, which is suitable for use in systematic reviews (106) and has been validated (107). Items relating to interventions were dropped as they were not relevant to any included study. Thus, the amended Downs & Black checklist included ten items assessing study reporting, two items assessing external validity, three items assessing internal validity (bias), three items assessing confounding (selection bias), and one item assessing whether there was a justification for the sample size used (power). Studies were classified as good quality if they scored sixteen or over out of a possible nineteen; poor quality studies scored ten or less. Moderate quality studies scored eleven to fifteen. Studies scored poorly for: reporting if they scored six or under out of a possible ten; internal validity (bias) and confounding (selection bias) if they scored one or under out of a possible three; external validity if they scored one or under out of a possible two; and if they did not include a justification for the sample size used.

2.1.4 Procedure

The literature search, screening, data extraction and quality assessment were carried out by LS, with guidance from GJR and JY. Predictors were grouped according to categories identified by Bish and Michie in a review of factors associated with vaccination for pandemic influenza (90). I report results for discrete categories in the results section in order of strength of association.

2.1.5 Registration

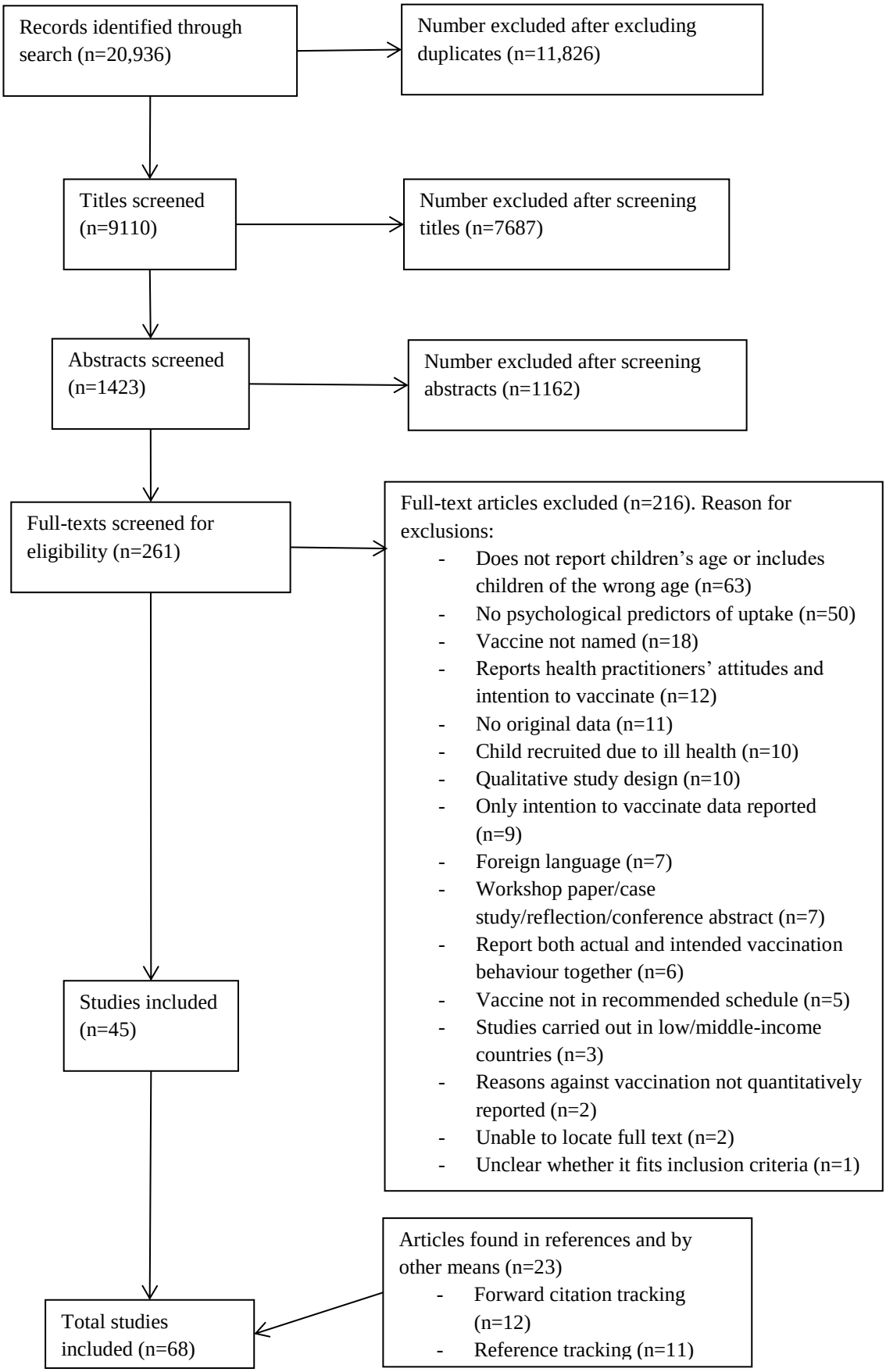
I registered the protocol for this systematic review on PROSPERO (CRD42016037983) (108).

2.2 **Results**

2.2.1 Study characteristics

Following screening (Figure 1), sixty-eight citations were included in the review, describing sixty-four studies. Studies were conducted in twelve countries and investigated thirteen vaccines. Thirty-seven studies used cross-sectional designs, fifteen used case-control designs and twelve used cohort designs.

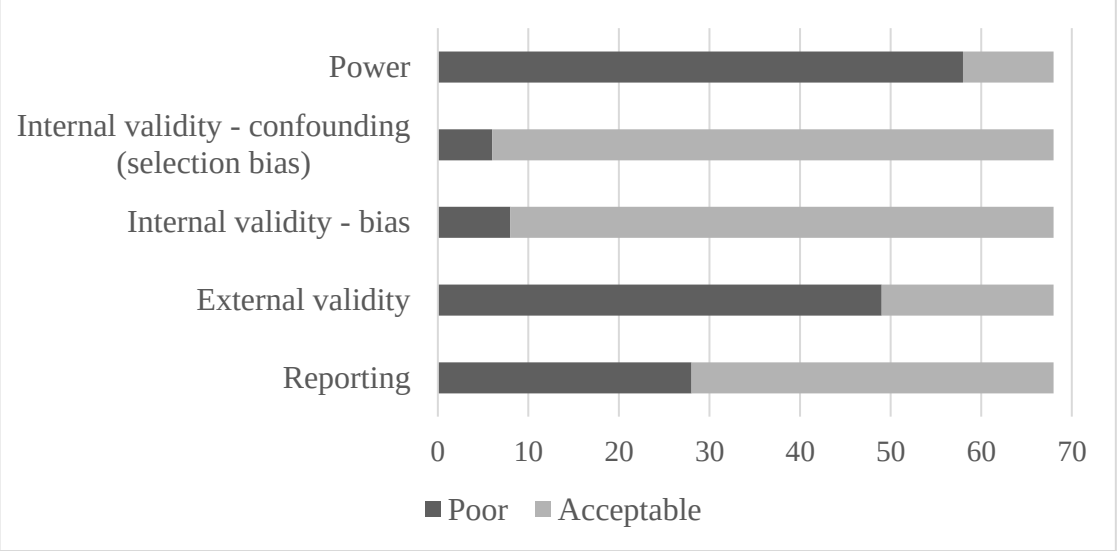
Figure 1. Flowchart depicting the selection of studies included in the systematic review of factors associated with vaccine uptake with reasons for exclusion



2.2.2 Risk of bias

Scores on the amended Downs and Black checklist (105) ranged between two and eighteen out of a possible nineteen, with a median score of thirteen. In terms of common issues within the literature, it was notable that only ten studies reported a power calculation (109-118). Forty-nine studies scored poorly for external validity (79, 109, 110, 112-115, 117-159); twenty-eight scored poorly for reporting (113, 115, 118-120, 122-125, 127, 132, 134, 136, 138, 140-142, 149, 151, 152, 156, 157, 159-166); eight scored poorly for internal validity (bias) (119, 120, 122, 123, 132, 137, 140, 159, 161); and six scored poorly for confounding (selection bias) (79, 120, 128, 129, 133, 149). Scores for individual studies are shown in the Appendix 1.

Figure 2. Chart indicating number of studies included in the systematic review of factors associated with vaccine uptake displaying different aspects of risk of bias



2.2.3 Psychological, social and contextual factors associated with uptake

Predictors and reasons given for or against vaccinating are summarised in Table 3 and Table 4 (for full tables see Appendix 1 and Appendix 2). Where relevant, only adjusted analyses are reported.

Table 3. Psychological, social and contextual factors associated with not vaccinating one's child

Factor	Psychological predictors of not giving child vaccinations / studies which investigated and did not find a significant association	Number of studies finding a significant association/Number of studies investigating the factor
Perception of adverse effects from vaccination	Vaccine is unsafe (111, 112, 115-117, 120, 125, 143, 144, 149, 157, 167) / (109, 153, 168)	12/15
	Vaccine causes side-effects (112, 113, 115, 130, 143, 157, 158, 160, 168-170) / (116, 139, 153)	11/14
	Child unwell at time of vaccine appointment (129, 139) /	2/2
	Belief that the vaccine is more dangerous than the illness (143); injections are traumatic to the child (144) /	2/2
	Can vaccinate child if they are ill (without fever) (157) / (167); child is often too ill to receive vaccinations (139, 158)	3/4
	Previous side-effects from vaccination (168) /(117, 126); negative previous vaccination experience (166)	2/4
Appraisal of the illness	Low perceived susceptibility to illness (109, 111, 120, 133, 143, 148, 150, 160, 169) / (130, 153, 171)	9/12
	Low perceived severity of illness (120, 121, 129, 143, 157) / (109-111, 126, 130, 137, 153, 160, 170, 171)	5/15
	Illness is dangerous (144) /	1/1
General beliefs and attitudes	Perception that it is not important for child to be vaccinated (112, 157, 160); vaccination is not useful (164); vaccines are not protective (170); no confidence in value of vaccines (149, 156) /	7/7
	Religious objection to vaccination (133, 139) /	2/2
	Negative attitude towards vaccination (114); do not agree with vaccination (155) /	2/2
Vaccine recommendations	No vaccine recommendation by health professional (110, 113, 125, 130, 143, 157, 164, 169) / (158)	8/9
	No vaccine recommendation by friends or family (110, 143) / (126)	2/3
	Government advice to vaccinate / (127)	0/1
	Health professionals' advice / (127)	0/1

Practicalities	Logistical barriers (150, 172); inconvenient time or place of vaccination (139, 171) / (113, 158); perceived time pressure (155)	5/7
	Expense of vaccine (113, 139) / (158)	2/3
	Vaccine course delivered in more doses (113) /	1/1
	Difficult to get the vaccine or appointment (117) / (113)	1/1
Knowledge	Incorrect knowledge (130, 153, 158, 171); confusion about the vaccination schedule (139); difficulty remembering vaccine schedule / (129)	5/6
	No knowledge about vaccination before appointment (109, 119) /	2/2
	Belief that the second dose of vaccine not essential (170) / (127); not important if a child misses a dose (172)	2/3
Social influences	Normative beliefs (113); subjective norms (143, 148) /	3/3
	Lack of perceived social approval of vaccination (79, 121) / (173)	2/3
Information about the vaccine	Less satisfaction with information given (119, 157); information thought to be unhelpful (127) /	3/3
	Information seeking behaviour (79) /	1/1
	Influence of information from the media (170) /	1/1
	No influence of information from the media (137) /	1/1
	Influence of research findings as important (127) /	1/1
	Influence of alternative/complementary medicine (157) /	1/1
	Faith in the media (126) /	1/1
	Less influence of healthcare provider (170) / (157)	1/2
	Perceived lack of information for vaccination decision (121) / (117)	1/2
	Adverse media publicity / (117)	0/1
Trust in the healthcare profession	Perception of a worse relationship with healthcare provider (149, 157) /	2/2
	No faith in the medical profession (112, 126) / (117, 156)	2/4
	Belief it is not right for health professionals to advise parents to vaccinate for the benefit of other children (121) /	1/1
	Lack of perceived clinical support (114) /	1/1
	Lower parental satisfaction with care / (117, 146, 147)	0/2
Perceived efficacy of vaccination	Vaccine is not effective (111, 120, 148-150, 157, 160, 172) / (110, 115, 129, 130, 144, 153, 170, 173)	8/16
Emotions	Worry about the vaccine (137, 151) /	2/2

	No fear that child will catch illness (143) /	1/1
	Anxiety about vaccination (143) /	1/1
	Inability to forgive oneself if child developed side-effects from vaccination (121); guilt about consequences / (126)	1/2
	Maternal psychological distress / (155)	0/1
Trust in the government	No trust in the government (112, 133) / (117)	2/3
	Belief there is a conspiracy (170) /	1/1
	Perceive government pressure to vaccinate / (127)	0/1
Multiple/combination vaccines	Appropriateness of separate vaccines over combination vaccines (112) /	1/1
	Combination vaccines are larger concern than single vaccines (121) /	1/1
	Combination vaccines are too much in one go (121) /	1/1
	Combination vaccines are harmful (170) /	1/1
	Children receive too many vaccines (157) /	1/1
	Not accepting multiple vaccines at once (117) / (113, 167)	1/3
	Multiple vaccines overwhelm the immune system (157) / (153, 172)	1/3
Preference for natural immunity	Belief that vaccination impairs body's natural immunity (143) /	1/1
	Preference for the child to get immunity naturally, through having the illness (121) /	1/1
	Belief that infections are good for the immune system (170) /	1/1
	Vaccines are unhealthy (126) /	1/1
Self-efficacy and perceived behavioural control	Belief it is not the government's responsibility to decide to vaccinate children (121) /	1/1
	Less perceived behavioural control (154); internal locus of control / (173)	1/2
	Self-efficacy / (172, 173)	0/2
Intention	Intention to vaccinate (113)	1/1

Table 4. Parental self-reported reasons for and against vaccinating child

Factor	Reasons given for not vaccinating	N	Reasons given for vaccinating	N
Perception of adverse effects from vaccination	Vaccine causes side-effects (79, 96, 110, 115, 116, 122-124, 130, 132, 137, 141, 152, 168)	14	Parents have been vaccinated without complication (119)	1
	Child was unwell at time of vaccination (115, 120, 122, 130, 132, 136, 141, 152, 162)	9	Won't harm the child even if vaccination does not benefit them (79)	1
	Vaccine is unsafe (115, 119, 162, 163)	4		
	Allergy to vaccine (79, 130, 132, 162)	4		
	Vaccines are dangerous (96, 144)	2		
	Previous side-effects: self (162); other person (165)	2		
	Concern about vaccination (131)	1		
Appraisal of the illness	Child has had the illness already (79, 120, 132, 136, 152)	5	Child is susceptible to illness (79, 165)	2
	Low perceived susceptibility to illness (110, 123, 124, 168)	4	Illness can be severe (79)	1
	Illness is not serious (116, 125, 168)**;** illness is harmless (119)	4	To prevent complications of illness (119)	1
	Complications of illness not frequent enough (125)	1		
	Parents have had the illness without harm (119)	1		
General beliefs and attitudes	Parental choice, did not want vaccination (96, 120, 130, 136, 162)	5	Vaccine is important (151)	1
	Vaccination is unnecessary (119, 130); vaccination is not useful (113)	3		
	Child is too young (130, 144, 162)	3		
	Disagree with immunisation (131)	1		
Vaccine recommendations	Advised against vaccination by health professional (120, 136, 141, 161)	4	Vaccine recommendation by health professional (79, 151)	2
	No vaccine recommendation by health professional (130);weak vaccination recommendation by health professional (125)	2	Vaccine recommendation by government (79)	1
	Negative influence of health visitor (137)	1		
Practicalities	Practical barriers (79, 96, 131); inconvenient time or place of vaccination (120, 122, 136, 162)	7		
	Appointment not offered or missed appointment (115, 120, 131, 136, 152, 162);	6		
	Expense of vaccine (113, 115, 125, 130)	4		
	Lack of time (130, 141, 163)	3		
	Vaccine out of stock (130, 141, 162)	3		

Knowledge	Inadequate knowledge about vaccine (130)	1		
	Incorrect knowledge about the vaccination schedule (both parent and physician) (110, 124, 130, 131, 138, 152)	6		
	Lack of knowledge where to get vaccine (130)	1		
	Lack of prior knowledge (141)	1		
	Child was unwell (no fever or major illness) (115, 120, 122, 130, 132, 136, 141, 152, 162)	9		
	Previous dose is still effective (130); one dose of vaccine is enough (137)	2		
Social influences	Other parents don't vaccinate child either (79)	1	Friends and family have accepted the vaccine (79)	1
Information about the vaccine	Adverse media publicity (79, 96, 124, 161)	4		
	Lack of information (163)	1		
	Lack of scientific data (141)	1		
	Heard problems with the vaccine (165)	1		
Trust in the healthcare profession	Doctors vaccinate without differentiation (144)	1	Trust in healthcare provider (144, 165)	2
Perceived efficacy of vaccination	Vaccine is not effective (79, 115, 130, 152)	4	To protect child from illness (119, 144)	2
			Trust in effectiveness of vaccine (79)	1
Emotions	Fear about vaccination (96, 120, 136)	3	Anticipated regret if do not vaccinate (79)	1
			Concern about child becoming ill (165)	1
Trust in the government	No trust in the government (79)	1	Required by law (151)	1
			Child receives vaccines according to National Immunisation Program (79)	1
Multiple/combination vaccines	Child receiving too many injections (116, 168); child receiving enough injections (124)	3		
	Did not want child to have vaccines all at once (162)	1		
Preference for natural immunity	Preference for natural immunity (123, 152)	2	Vaccination will strengthen the child's immune system (119)	1
	Illness strengthens child's immune system (119)	1		
	Illness is beneficial for child (119)	1		
	Prefer to use homeopathic alternative (79, 162)	2		
Intention	Postpone vaccination to a later date, intend to vaccinate child later (110, 122, 124, 152, 168)	5		

2.2.3.1 *Perception of adverse effects from vaccination*

There was strong evidence for an association between perception of adverse effects and vaccination. Self-reported reasons for not vaccinating included: believing the vaccine to cause side-effects (79, 96, 110, 115, 116, 122-124, 130, 132, 137, 141, 152, 168) or to be unsafe (115, 119, 162, 163); believing one's child to be allergic to the vaccine (79, 130, 132, 162); previous experience of the child or someone else experiencing side-effects (162, 165); believing that vaccines are dangerous or cause trauma (96, 144); and being concerned about the child becoming ill due to vaccination (165). Although recommendations state that children can be vaccinated if they are mildly ill (174), parents in nine studies reported not vaccinating their child because they were unwell (115, 120, 122, 130, 132, 136, 141, 152, 162). Reasons for vaccination included that parents themselves had been vaccinated without complication (119) and that vaccination would not harm the child even if it did not benefit them (79).

Twelve of fifteen studies found an association between perceiving vaccination to be unsafe and vaccine refusal (111, 112, 115-117, 120, 125, 143, 144, 149, 157, 167). Four studies were good quality (111, 116, 117, 167); all those not finding an association were moderate quality (109, 153, 168). Eleven of fourteen studies found an association between perceiving a vaccine to cause side-effects and vaccine refusal (112, 113, 115, 130, 143, 157, 158, 160, 168-170). All fourteen were moderate or good quality. An association was found between vaccine refusal and the child being ill at the time of vaccination (129, 139) and the belief that the child was often too ill to receive vaccinations (139, 158). One study found that believing a child cannot be vaccinated if they are ill without a fever was associated with vaccination status (157), whereas another did not (167). These were moderate and good quality respectively. Another study found an association between vaccine refusal and believing that vaccination was more dangerous than the illness (143).

2.2.3.2 *Appraisal of the illness*

There was strong evidence for an association between perceived susceptibility to an illness and child vaccination, however the link with perceived severity of the illness was tenuous. In terms of self-reported reasons against vaccination, studies

variously identified a belief that the child had already had the illness (79, 120, 132, 136, 152); perceived low severity of the illness (116, 119, 125, 168); perceived low susceptibility to the illness (110, 123, 124, 168); belief that complications of the illness were not frequent enough (125); and belief that the parents had had the illness without harm (119). Conversely, reasons for vaccinating included believing the child to be susceptible to the illness (79, 165); that the illness could be severe (79); and to prevent complications of the illness (119).

Twelve studies investigated the association between perceived susceptibility to illness and vaccination, with nine finding a significant association (109, 111, 120, 133, 143, 148, 150, 160, 169). Most studies were moderate quality, with one good quality study (111) and one poor quality study (120). Fifteen studies investigated the association between perceived severity of the illness and child vaccination, with five finding an association (120, 121, 129, 143, 157). Studies that found no association were generally better quality, with four good quality studies (110, 111, 170, 171).

2.2.3.3 *General beliefs and attitudes*

There was good evidence for an association between parental beliefs and attitudes and child vaccination. Self-reported reasons against vaccination included thinking that vaccination was not necessary or useful (113, 119, 130); and disagreeing with immunisation (131). Parental reasons for vaccinating included perceiving the vaccine to be important (151).

Beliefs and attitudes positively associated with uptake included believing the vaccine to be important or useful; believing it to be protective; having confidence in the value of vaccines; holding a positive attitude towards immunisation; agreeing with vaccination; and not having religious objections to vaccination. All eleven studies investigating these beliefs and attitudes found a significant association with uptake (112, 114, 133, 139, 149, 155-157, 160, 164, 170). All were moderate quality, apart from two high quality (114, 170) and one poor quality (149) studies.

2.2.3.4 *Vaccine recommendations*

Across multiple studies, parents reported not vaccinating their child because: they were advised against vaccination (120, 136, 141, 161); did not receive a vaccine recommendation by a health professional (130); received a weak vaccination recommendation from a health professional (125); or because a health visitor had a negative influence (137). Two studies reported that parents vaccinated their child because they received a recommendation from a health professional or the government (79, 151).

Of the ten studies investigating receiving vaccine recommendations from a health professional, friend or family member, eight found an association with uptake (110, 113, 125, 130, 143, 157, 164, 169). One study was good quality (110), while others were moderate quality. The two studies which did not find an association were both moderate quality (126, 158).

2.2.3.5 *Practicalities*

Seven studies reported practical barriers, inconvenient timings or clinic locations as reasons against vaccination (79, 96, 120, 122, 131, 136, 162); six cited missing or not being offered an appointment (115, 120, 131, 136, 152, 162); four cited the expense of the vaccine (113, 115, 125, 130); and three each cited a lack of time (130, 141, 163) and the vaccine being out of stock (130, 141, 162).

Perceiving logistical barriers towards vaccination; inconvenient appointment location or time; and time pressure were investigated as risk factors by seven studies, of which five found an association with refusal (139, 150, 155, 171, 172). Two were good quality (155, 171). Both studies which found no association were moderate quality (113, 158). Having to pay for the vaccine was associated with vaccine refusal in two studies (113, 139), while one (158) found no association; all were moderate quality. Perceiving it to be difficult to get the vaccine or a vaccination appointment was associated with not vaccinating in one of two studies (117); as was having a vaccine course delivered in multiple doses (113).

2.2.3.6 *Knowledge*

Overall, there was good evidence for an association between increased knowledge about the vaccine and uptake. Six studies reported that parental

reasons against vaccination included incorrect knowledge of the vaccine schedule by the parent or physician (110, 124, 130, 131, 138, 152). Perceived inadequacy of knowledge about the vaccine or where to get it (130, 141) and believing that previous doses of the vaccine were still effective or that one dose was enough (130, 137) were also self-reported reasons for not vaccinating.

Six studies found an association between vaccine refusal and incorrect knowledge, confusion or difficulty remembering the vaccination schedule (130, 139, 153, 158, 171); or not knowing about the vaccination before the appointment (119). Of these, one study was good quality (171), one was low quality (119) and the rest were moderate quality. One moderate quality study found no association between difficulty remembering the vaccine schedule and vaccination (129). Not believing that it was important if a child missed a vaccination dose, or that the second dose was not essential was associated with uptake in two of three studies (170, 172). Studies finding an association were good (170) and moderate quality (172); the study not finding an association was also moderate quality (127).

2.2.3.7 *Social influences*

There was mixed evidence for an association between social influences and vaccination. Parents' self-reported reasons against vaccination included that other parents did not vaccinate their child (79), while reasons for vaccinating included that friends and family had vaccinated their child (79).

Two moderate quality studies found an association between lack of perceived social approval of vaccination and vaccine refusal (79, 121), whereas one good quality study did not find an association (173). Subjective norms were associated with vaccine uptake (143, 148), as were normative beliefs (113).

2.2.3.8 *Information about the vaccine*

There was some evidence for an association between information about the vaccine and vaccination, whereas there was mixed evidence for the direction of the association between the influence of the information source and vaccination. Studies indicated that parents reported not vaccinating their child because of adverse media publicity (79, 96, 124, 161); perceived lack of information (163); lack of scientific data (141); and having heard there were problems with the vaccine (165).

Three studies found an association between vaccine uptake and whether parents were satisfied with the information provided or thought it helpful (119, 127, 157). One of two studies investigating perceived lack of information and vaccine refusal found an association (121). Information seeking behaviour was associated with vaccine refusal (79). No association between vaccination and adverse media publicity was found in a good quality study (117).

Increased influence of information disseminated by the media was associated with both vaccine uptake (137) and refusal (170). The study finding an association with vaccine refusal was better quality. Faith in the media (126), influence of a provider of alternative or complementary medicine (157), and perceiving research findings to be important (127) were associated with vaccine refusal. An association between influence of information from a healthcare provider and child vaccination was also found by one study (170), but was not replicated in another lower quality study (157).

2.2.3.9 *Trust in the healthcare profession*

There was mixed support for an association between child vaccination and trust in the healthcare profession. One study reported that parents did not vaccinate their child because they believed that doctors vaccinate without differentiation (144). Parents in two studies gave trusting their healthcare provider as a reason for vaccination (144, 165).

An association between uptake and faith in the medical profession was found by two of the four studies which investigated it (112, 126); both were moderate quality. One of the two studies which did not find an association was good quality (117). Two studies found an association between better perceived relationship with the healthcare provider and vaccination (149, 157); perceived clinical support was also associated with vaccination (114). Parental satisfaction with care was not associated with vaccination in either of two studies (117, 146, 147), one of which was good quality (117).

2.2.3.10 *Perceived efficacy of vaccination*

Evidence for an association between perceived efficacy and child vaccination was mixed. Not believing that the vaccine was effective was reported by parents as a reason against vaccination in four studies (79, 115, 130, 152). Two studies found

that parents vaccinated their child to protect them from the illness (119, 144), and another cited trust in the effectiveness of the vaccine (79).

Perceived efficacy was found by eight studies to be associated with child vaccination (111, 120, 148-150, 157, 160, 172). Of these, two were poor quality (120, 149) and one was good quality (111). Eight more studies found no significant association (110, 115, 129, 130, 144, 153, 170, 173), including three good quality studies (110, 170, 173).

2.2.3.11 *Emotions*

There was good evidence for an association between parental emotions about the vaccine and uptake. Four studies cited fear of or concern about the vaccination as a self-reported reason against vaccination (96, 120, 131, 136). Reasons for vaccination included anticipated regret if parents refused vaccination and their child developed the illness (79),

Studies investigating parental worry about vaccination (137, 151); fear of the illness (143); and anxiety about vaccination (143) all found an association with vaccine refusal. One study investigating maternal psychological distress did not find an association (155). Two studies investigated feelings of guilt or the inability to forgive oneself if the child developed side-effects from vaccination (121, 126). Only one found an association (121); both were similar quality.

2.2.3.12 *Trust in the government*

Taken together, there was weak evidence for an association between trust in the government and child vaccination. Parents in one study reported not vaccinating their child because they did not trust the government (79). Parental self-reported reasons for vaccination included because it was required by law (151) and because the child received vaccines according to the national immunisation programme (79).

An association was found by two of three studies that investigated trust in the government and child vaccination (112, 133). Both were moderate quality, however, the study not finding an association was good quality (117). Belief that there was a conspiracy was also associated with vaccine refusal (170), whereas

the perception that there was government pressure to vaccinate was not associated with vaccination (127).

2.2.3.13 *Multiple/combination vaccines*

There was mixed evidence of an association between negative perceptions surrounding multiple vaccination and uptake of combination vaccines. Three studies reported that parents did not vaccinate their child because they felt that they received too many or enough injections (116, 124, 168); another reported that parents did not want the child to have multiple vaccines at once (162).

One study found an association between vaccine refusal and the belief that children receive too many vaccines, and that multiple vaccinations overwhelm the immune system (157), whereas two studies found no association (153, 172). Similarly, only one of three studies found an association between not accepting multiple vaccines in a single appointment and vaccine refusal (117). Although this was a good quality study, one of the studies that did not find an association was also good quality (167), whereas the other was moderate quality (113). The perception that combination vaccines were a greater concern than single vaccines and were too much to give the child in one go (121); that combination vaccines were harmful (170); and that separate vaccines were more appropriate than combination vaccines (112) were also associated with vaccine refusal.

2.2.3.14 *Preference for natural immunity*

There was some evidence for an association between parents' preference for natural immunity and vaccine refusal. Parental reasons against vaccination included having a preference for natural immunity (123, 152) or a homeopathic alternative (79, 162); and believing that having the illness was beneficial for the child and strengthened their immune system (119). Parents' reasons for vaccinating also included wanting to strengthen the child's immune system (119).

An association was found between vaccine refusal and parents' preference for acquiring immunity through illness over vaccination (121); believing that infections are good for the immune system (170); believing that vaccination impairs natural immunity (143); and believing that vaccines were unhealthy (126). All studies were moderate quality bar one, which was good quality (170).

2.2.3.15 *Self-efficacy and perceived behavioural control*

Generally, there was weak evidence for an association between self-efficacy and perceived behavioural control and child vaccination. Perceived behavioural control was associated with vaccination in one moderate quality study (154), whereas locus of control was not associated with vaccination status in a good quality study (173). Two studies investigating the association between self-efficacy and child vaccination found no association (172, 173).

2.2.3.16 *Intention*

Parents of unvaccinated children reported intending to vaccinate their child in the future in five studies (110, 122, 124, 152, 168).

One longitudinal study found that intention to vaccinate one's child was associated with subsequent behaviour (113).

2.2.3.17 *Combined effects*

Some studies investigated the combined effects of predictive factors on uptake of childhood vaccinations. In these cases, it was impossible to tease out how each factor affected uptake. An association between vaccination and immunisation-related beliefs (114); attitude score (136, 154); vaccine efficacy and vaccination attitudes (143); lack of perceived vaccine harms (156); and lack of belief in disease susceptibility and severity, and vaccine effectiveness (117); knowledge and vaccine practice (118) was found. A lower score on the 'parent attitudes about childhood vaccines' survey, which identifies vaccine hesitancy through measuring perceived vaccine safety, efficacy and vaccination attitudes was also associated with vaccine uptake (135). Concern about the vaccine and potential adverse effects was associated with vaccine refusal (152), as was a lower number of cues to action (148).

Some studies analysed multiple beliefs, attitudes and dimensions within the combined context of perceived barriers and benefits to vaccination. Among studies investigating perceived barriers to vaccination, one study of good quality which used eleven items to measure barriers to vaccination (173), two studies of moderate quality, which used five and six items respectively (134, 148, 173) and a low quality study using fourteen items (140, 159) found an association between

perceived barriers and vaccination refusal. One good quality study, measuring perceived barriers on a four-item scale did not find an association between perceived barriers and child vaccination (110). One moderate quality study, investigating the association between perceived benefits and vaccine uptake, found an association (156). This study used four items, investigating efficacy and safety of the vaccine as well as attitudes, to measure perceived benefits. However, a good quality study, which used 'one or two items' did not find this association (171).

2.2.3.18 *Other*

Parents' self-reported reasons for not vaccinating their child included not wanting the vaccine (96, 120, 130, 136, 162); not knowing about or refusing the vaccine (115); deciding against the vaccine after having had one or more doses (138); not knowing whether to vaccinate and not having thought about vaccination (130); vaccination no longer being mandatory (152); the child never getting ill (79); or rarely going out (130); or perceiving the vaccine to be an adjuvant (enhancing the body's natural immune response) (123). Parents did not vaccinate their child because they should have been vaccinated in school, but there was no record of the vaccination and parents did not recall whether their child had been vaccinated or not (131) and because the mother had been vaccinated for the illness (144). Reasons given by parents for vaccination included doing so because their child had a chronic disease (79, 119); there was a vulnerable person in household (79); and it was required by the day care the child attended (151).

Perceiving the child to be too young (130, 144, 162); having a previous negative vaccination experience (166) or having previously refused a vaccine for reasons other than ill-health (168); having fewer general problems during immunisation (114); and having difficulty remembering the vaccination appointment (158) were associated with vaccine refusal. No feelings of doubt, but more negative feelings experienced following the vaccination decision were associated with vaccine uptake (79).

Some studies yielded contradictory results. Parental acculturation to the host country was found to be associated with both vaccine uptake (142) and vaccine refusal (145). Uptake was also associated with the belief that it was easier to be

told whether or not to vaccinate your child (121) and that parents had the right to determine the treatment given to their child (144). Both were moderate quality studies.

2.3 Discussion

This is the first comprehensive review describing psychological, social and contextual factors associated with vaccination in young children. In line with findings from previous reviews of child vaccination (91, 93) and wider reviews of medication adherence (175), perceiving vaccination to cause adverse effects was consistently associated with vaccine refusal. Many high-quality papers (111, 116, 117, 167) found this association and it was the most common self-reported reason against vaccination. While there was strong evidence for an association between low perceived susceptibility to an illness and vaccine refusal, evidence for a role of perceived illness severity was weak. This may be because parents first consider whether their child is susceptible to an illness before considering how severe the illness may be.

Few studies have investigated information about vaccination or the influence of different sources of information, with inconsistent results. Although parental satisfaction with information was associated with vaccine uptake (119, 157), information seeking behaviour was associated with vaccine refusal (79). One possible explanation is that parents' distrust of information causes them to seek information from multiple sources, including the internet and social media (176). Unfortunately, many websites perpetuate vaccine 'myths' (177). Likewise, influence of information disseminated by the media (in newspapers, magazines and on the television) was associated with vaccine uptake (137) and refusal (126, 170). No studies included in the review investigated the influence of social media on vaccine uptake, even though it likely affects vaccination behaviour in certain countries. This is perhaps due the fact that social media is a relatively new phenomenon. More research is needed on the influence of information to improve the content and dissemination of public health messages.

I found no experimental studies which investigated whether interventions to alter parental beliefs and attitudes affected vaccine uptake in children aged five and under. This is a logical next step for child vaccine uptake research. Although

research on interventions to change parental beliefs about and attitudes towards vaccination have been conducted (178), outcomes are usually measured as a change in attitudes or vaccination intentions (179). Some intervention studies have investigated the impact of additional vaccine reminders through new modes of communication, such as text message reminders (180, 181), but very few have investigated the effectiveness of different messages in increasing vaccination (179). My review highlights factors which could be targeted by such messages.

Since having conducted the review, a systematic review of factors associated with influenza vaccine hesitancy in all age groups has been published (182). This review identified 470 studies which investigated influenza vaccine hesitancy, of which eighteen investigated vaccination in children under the age of five. Vaccine hesitancy was defined by the study as low vaccination intention or vaccination refusal. This review identified similar barriers to child seasonal and pandemic vaccination as I found in my review, including: higher perceived risk of side-effects from vaccination; worry about the safety of the vaccine; perceived low severity of influenza; perceived low susceptibility to influenza; belief that the vaccine is ineffective; low perceived behavioural control; lack of general knowledge about influenza; past vaccination behaviour; perceiving vaccination to be inconvenient; fewer interactions with the healthcare system; and no direct recommendation from a healthcare professional.

As we have seen, there is a wealth of research investigating vaccine uptake in various disciplines, including public health, psychology and sociology, but little research integrating different disciplines (179). Interdisciplinary research may help shed light on mechanisms underlying vaccination behaviours. For example, biases and heuristics are known to exert a significant influence on vaccination behaviour (101, 102). Common biases affecting vaccination identified in the literature include: the omission bias, in which the negative consequences of action are considered worse than the negative consequences of inaction (101, 102, 183-186) and the availability bias, whereby judgements about the probability of an incident occurring are based on the availability with which examples of that incident come to mind (101, 102, 184, 185). In the vaccine literature, the term ‘cognitive bias’ tends to refer to these processes of thinking and reasoning which are associated with vaccination behaviour. However, ‘cognitive biases’ is also

used to refer to biases in information processes such as attention, interpretation and recall, and can be defined as ‘the tendency to attend to a certain type of stimulus or consistently interpret emotionally ambiguous information in one direction’ (187) (p. 516).

One of the key differences between ‘cognitive biases’ as used in the vaccine literature and cognitive biases of information processing is the influence of emotional valence in the latter. Cognitive biases of information processing manifest as systematic patterns of attention, interpretation and recall in response to emotionally valenced stimuli. These biases have been heavily implicated in vulnerability to emotional disorders, such as depression and anxiety (188, 189). Biases can influence behaviour by promoting selective attention to, and interpretation and recall of, specific emotional material associated with the behaviour. Cognitive biases can be modified, often resulting in changes to attitudes and behaviour. This makes cognitive biases an important option to explore with regard to child vaccination behaviour. Unless otherwise stated, use of the term ‘cognitive biases’ in the remainder of this thesis refers to cognitive biases of information processing.

Cognitive psychology indicates that one specific subset of the cognitive bias phenomena may be particularly relevant in parental vaccination behaviour, namely interpretation bias. The term ‘interpretation’ has a very precise meaning within cognitive psychology and has been defined as ‘the process through which one meaning is extracted from ambiguous information in order to construct a mental representation’ (190) (p.562). This is distinguished from the related, but cognitively distinct, processes of judgement, reasoning and decision making. Interpretation *bias* is defined as ‘a consistent tendency to interpret emotionally ambiguous stimuli, situations, or events in a negative (or positive) manner’ (191) (p. 26). Interpretation bias has the potential to promote the selective processing of material which is likely to trigger or maintain the behaviour (192). A systematic bias in interpretation that acts specifically upon vaccination-relevant information could either promote or inhibit behaviours related to vaccination uptake. Thus, cognitive biases could act as a mechanism underlying vaccination behaviour. However, no studies investigating the association between vaccination and information processing biases were included in the systematic review.

One characteristic of information processing biases is that they act specifically on information that matches the core concerns of the sample under study, a phenomenon known as content-specificity (193). Vaccination is an emotionally ambiguous health intervention which can be interpreted as a positive, protective intervention, or as posing a significant health threat through potential adverse effects (102). When considering potential associations between cognitive biases and child vaccination behaviour, it is likely that biases about the type of health threats associated with child vaccination will show the strongest association with vaccination behaviours.

Two domains might be particularly relevant in child vaccination. First, when deciding whether to vaccinate their child, parents must weigh up the relative threats posed by the 'unnatural' man-made vaccine and the naturally-occurring illness (102). Two factors identified in the systematic review are relevant here. Parents' belief that the vaccine could cause adverse effects would be included in their interpretation of man-made health threats, while parents' appraisal of the illness would be included in their interpretation of naturally-occurring health threats. Man-made threats tend to elicit higher levels of concern than naturally-occurring threats (194). This is a common finding in the risk perception literature, with the degree to which the threat 'interferes with nature' or is perceived as being 'unnatural,' greatly impacting on risk perception (195, 196). Some parents may perceive natural interventions as preferable to artificial, man-made interventions. Evidence shows that endorsement of natural interventions is associated with vaccination refusal (102, 197). Thus, parents may have different interpretation biases based on the source of the health threat. It is likely that parents will have more negative interpretation biases for man-made health threats, such as the influenza vaccine, than for naturally-occurring health threats, such as influenza itself.

Second, child vaccination is potentially unusual as a public health behaviour in that it represents a threat to someone other than oneself (one's child). While cognitive biases are generally investigated in oneself, research indicates that parental negative biases carry over into ambiguous situations involving one's child (198-200), although results are weaker than in situations involving the self (198, 199). Therefore, parents may have different interpretation biases based on

the subject of the health threat. It is likely that parents will have more negative interpretation biases for threats to their own health, than for threats to their child's health.

While the influence of cognitive biases is well-researched in emotional disorders such as anxiety and depression (188, 201), there is little research investigating the influence of cognitive biases on the adoption of public health behaviours. These studies investigate interpretation bias and attention bias – the systematic tendency to attend to emotionally valenced stimuli over neutral stimuli (202). Content-specific interpretation biases have been associated with problem drinking (203, 204), while content-specific attention biases have been associated with lapses in a smoking cessation attempt (205) and with being overweight (206). However, the role of attention biases in consummatory behaviours (such as excessive eating and drug or alcohol misuse) is mixed, with evidence indicating that biases are not consistently associated with body weight, food consumption or substance use (207). One study, investigating the association between attention bias and medication adherence may shed light on how cognitive biases could influence child vaccination. This study found that both those low and high in asthma medication adherence showed increased attention bias for asthma-symptom words (208). This pattern of results is in line with evidence suggesting that the emotional valence of stimuli is associated with biased processing (188), but suggests that the impact of biases on public health behaviours can be beneficial or maladaptive based on individual differences (208). In the case of child influenza vaccination, underlying cognitive biases may influence parents' vaccination decision, with biases being most evident in those who strongly agree or disagree with vaccination.

2.3.1 Limitations of the literature

First, studies included in the systematic review varied in quality and reported different details of methods used. For example, some studies defined 'vaccinated' by specifying a number of vaccine doses, a time frame and how it was ascertained that the child was vaccinated, while others simply stated that children 'were vaccinated.'

Second, papers also differed in factors adjusted for in their analyses.

Third, most included studies were cross-sectional, therefore causal inferences between psychological predictors and vaccine uptake can only be made with caution. However, twelve cohort studies were included in the review. More prospective longitudinal or intervention studies are now needed.

2.3.2 Limitations of the review

First, demographic predictors of vaccination and qualitative research were excluded from the review for pragmatic reasons, meaning some potential predictors of vaccination may have been overlooked. However, reviews of qualitative literature investigating child vaccination yield similar results to those found in this review (91).

Second, results were not split by vaccine. Differing strengths of association between factors and particular vaccines may exist.

Third, some studies investigated differences between parents who did not vaccinate their child on time and those who did not vaccinate their child at all (e.g. (115, 209)). I did not differentiate between these outcomes. It may be that important differences exist between hesitancy and refusal that could be studied by future research.

Fourth, literature not published in English was excluded due to time and cost constraints. Grey literature was not searched for the same reasons. This increases the risk that I did not identify some studies that reported largely non-significant findings.

Finally, as one person carried out the review, data extraction and risk of bias assessment, I cannot rule out human error or experimenter bias.

2.3.3 Conclusions

This is the first systematic review identifying psychological predictors of uptake of routine child vaccinations. My results indicate that the factor most consistently associated with vaccine refusal is concern about potential adverse effects of the vaccine. The child's susceptibility to the illness and the belief that the vaccine is effective are also likely to be relevant predictors of uptake. Increasing parents' knowledge of the vaccine schedule and ensuring all healthcare providers recommend vaccination may also be associated with uptake. More research on the

influence of different sources of information is needed to determine the best way to disseminate information about vaccines to parents. Underlying parental cognitive biases may also influence the parental vaccination decision, however as no research exists, the extent of the association remains unclear.

Chapter 3. Systematic review of factors affecting parental perception of symptoms

In Chapter 2, I found strong evidence that parents who believe that vaccines cause side-effects are less likely to vaccinate their child. This is a particular problem for the child influenza vaccine as children must be vaccinated each year and clinical trial data indicate that 40% to 50% will report at least one side-effect (77, 78). Although acute symptoms are common following many vaccinations, their cause is not always straightforward. As noted in Chapter 1, a recent clinical trial comparing Fluenz Tetra to placebo found that 41.7% of participants who received the drug reported side-effects, as did 40.6% in the placebo arm; there was no statistical difference in side-effect reporting between the two groups (78). It therefore cannot be concluded that the pharmacological properties of Fluenz Tetra are the source of symptoms perceived following vaccination.

The finding that there is no difference between the proportion of people reporting side-effects in the active and sham arms of the Fluenz Tetra clinical trial is not an isolated occurrence in the literature. Many clinical trials of medications used for a range of conditions have found no difference between rates of adverse effects reported in the placebo and active arm, despite a common perception that the drug in question causes side-effects. For example, a meta-analysis comparing adverse events in the intervention and placebo arms of statin trials indicated that symptoms commonly perceived as side-effects from statin were perceived just as frequently in the placebo arm as in the intervention arm (placebo: 0.1%-17.7%, active drug: 0.1%-18.1% depending on the specific symptom) (210). Similarly, in a meta-analysis of fifty-three trials for migraine medication in adults, the incidence of adverse events in the active drug arm was similar to placebo for four of the twelve drug-dosage combinations investigated (211). Less research has been conducted in children, but where it has, results are analogous. For example, a systematic review of ten trials for migraine medication in children found that for four of five drugs prescribed (acetaminophen, ibuprofen, rizatriptan, dihydroergotamine; not sumatriptan), adverse events were seen just as frequently

in the placebo and active drug arm of the study (placebo: 1.6%-8.3%, active drug: 1.2%-16.7% depending on the medication and the specific symptom) (212).

Not only are side-effect rates often similar in the active and sham arms of randomised-controlled trials for a given drug, but the side-effect profiles experienced by participants in placebo-controlled trials are similar to those experienced by those in the active drug arm. A recent meta-analysis of 231 randomised, placebo-controlled trials investigating a variety of disorders in those aged sixteen and over found that reporting of adverse events in the placebo and active drug arm was highly correlated for most symptoms (213). This pattern has also been found in other reviews of clinical trials for specific disorders. For example, a systematic review of seventy-three placebo-controlled trials for migraine medication found that participants in the placebo condition experienced a symptom profile similar to that of the class of drug they thought they were taking (non-steroid anti-inflammatory drugs (NSAIDs), triptans and anticonvulsants) (214). Likewise, in a systematic review of 143 trials for antidepressant medications, the symptom profile experienced in the placebo arm of trials for tricyclic (TCA) medications was different to that experienced in the placebo arm of selective-serotonin reuptake inhibitor (SSRI) medications; symptoms experienced in the placebo arm matched the side-effect profile in the active drug arm for the respective class of antidepressant (215, 216). A similar pattern of adverse events in the placebo and active drug arms has also been found in a meta-analysis of treatments for fibromyalgia (217) and, though no statistical comparison was made, analogous results are presumed for Parkinson's disease treatment trials (218).

If side-effects attributed by patients to a particular medication are equally likely to be triggered by a sham medication, it is clear that the symptoms are not necessarily caused by the pharmacological action of the drug. What, then, is their cause? One possibility is the nocebo effect, a phenomenon whereby the expectation that symptoms will develop following exposure to an inert substance becomes self-fulfilling (214, 218, 219). A recent systematic review of 89 studies found that three factors were particularly influential in triggering a nocebo response, namely: having seen or heard suggestions that an exposure causes symptoms; having higher expectations of symptoms; and increased dose of

exposure (220). As such, adverse effects seen in the placebo arms of trials may arise from participant expectations about side-effects that they might experience, including patients' prior experience with similar medications (214, 215).

The literature on medically unexplained symptoms may also provide some insight into the origin of symptoms that are attributed to medications. Definitions of medically unexplained symptoms vary, but they are generally understood as the presence of symptoms which cannot be linked to a medically diagnosed cause (221, 222). Some symptoms are commonly experienced together and have come to be referred to as 'functional syndromes,' for example chronic fatigue syndrome, fibromyalgia and irritable bowel syndrome (223). Medically unexplained symptoms are common, with estimates indicating that 19% (224) to 66% (225) of symptoms in primary care are unexplained. The wide range in prevalence estimates is likely due to differing definitions of what counts as 'unexplained.' Medically unexplained symptoms persist into secondary and tertiary care, with as many as 52% of new patients referred by their primary clinician to outpatient clinics in hospital being thought to have at least one medically unexplained symptom (222). Unexplained symptoms are likely to recur or be chronic in at least one in five patients (223), with a longitudinal study indicating that symptoms in over one-third of patients presenting to a primary care clinic remained medically unexplained after five years (226). In some cases, medically unexplained symptoms may be the physical manifestation of psychological disorders (222). As with the nocebo effect, the literature on medically unexplained symptoms has focussed on how psychological processes can result in patients identifying symptoms in themselves and how these symptoms are then interpreted and maintained.

Limited research has been conducted on the psychological or contextual factors that affect perception of symptoms in one's child. However, literature relating to the nocebo effect and medically unexplained symptoms in oneself may cast light on possible mechanisms that may be involved when a parent comes to perceive side-effects in their child following vaccination. A number of models have been put forward which attempt to explain symptom perception in oneself. In the following sections I review existing models of symptom perception and factors underlying subjective symptom perception with the aim of identifying factors that

may influence parental perception of side-effects in one's child following vaccination. I then describe a formal systematic review of the factors associated with parental perception of symptoms in one's child.

3.1 Models of symptom perception

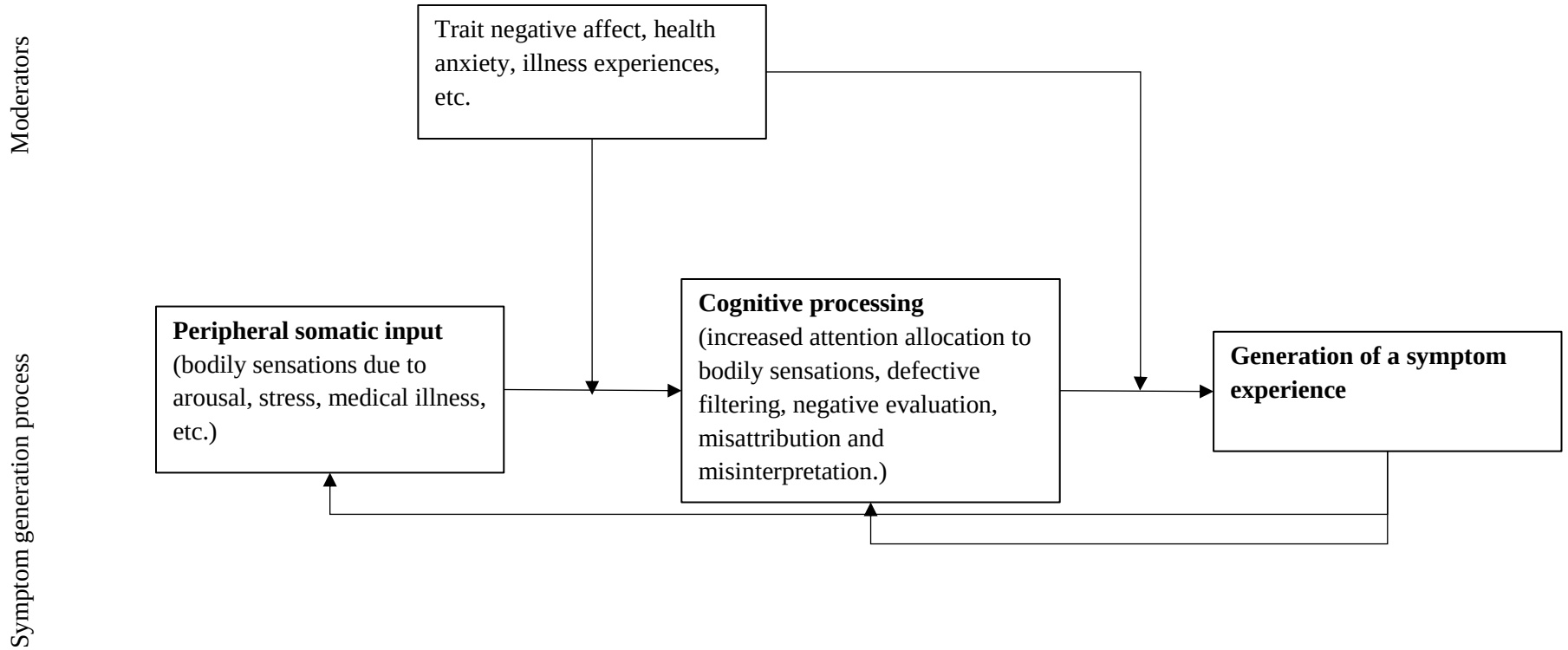
Physical symptoms were initially thought to occur following certain biological processes, assuming a correspondence between the pathology and the symptom, as well as between the severity of the pathology and the severity of the symptom (227). However, symptom perception is now thought to be a more complex process, with convincing evidence that psychological factors, such as the wider context, behaviour of others, and beliefs and attitudes held, are important (227). The perception of pain, for example, is not linearly related to the activation of primary sensory neurons, with multiple factors such as genetics, cognitions and emotions affecting neural signals (228). In addition, a range of cognitive processes, such as attention to bodily sensations and interpretation of sensations as benign or malignant, play an integral part in symptom perception (229). Attention and interpretation have been implicated in the perpetuation of symptoms as well as initial symptom perception (230).

The influence of cognitive processes on symptom perception was first highlighted by Pennebaker (229) and has given rise to a number of models, such as the cognitive-perceptual model (227) and the symptom perception model (231) which attempt to describe mechanisms underlying symptom perception in oneself. Models of symptom perception have also been put forward for medically unexplained symptoms (232-234), somatisation disorder (235) and asthma (236).

While models differ in the components included and associations suggested, the majority of models implicate attention and interpretation as part of symptom perception (see Van den Bergh et al. (233) for summary). A simple portrayal of the basic structure of these models is the modal model of symptom perception, seen in Figure 3 (237). Typically, there is an initial peripheral somatic input; these bodily sensations can arise from pathology, arousal, or stress. The next stage suggested by the model is cognitive processing, in which bodily sensations are attended to and interpreted, resulting in experience of a symptom. Symptom experience can in turn influence somatic input and further cognitive processing.

Psychological factors such as trait negativity, health anxiety, and learning may moderate the association between bodily sensations and cognitive processing, and between cognitive processing and symptom experience. For example, those with increased neuroticism, negative affect and anxiety attend more to bodily sensations and are more likely to interpret a sensation as threatening or malign (231, 238-240).

Figure 3. Modal model of symptom perception. Reproduced from “Symptoms and the body: Taking the inferential leap,” by O Van den Bergh et al., 2017, Neuroscience and Biobehavioural Reviews, 74 (Pt A), p. 187. Copyright 2017 by Elsevier. Reprinted with permission.



3.2 Factors affecting symptom perception in oneself

The modal model suggests that psychological and cognitive processes play a key role in subjective symptom perception. A wealth of evidence supports this and suggests avenues for investigation with regard to parental perception of symptoms. In the sections below, I review the main evidence for psychological factors underpinning subjective symptom perception.

3.2.1 Misattribution of existing symptoms

Subjective health complaints, including non-specific symptoms such as headache, pain and tiredness are commonly experienced in everyday life. Studies indicate that at least 75% of people aged fifteen and over reported experiencing symptoms in the last thirty days in Denmark, Sweden, Norway and Finland (241-243). This phenomenon has been long documented, with one study published in 1969 finding that 81% of a cohort of hospital staff and university students had experienced common symptoms; however, the time frame over which symptoms were perceived was not specified (244). While some might argue that the finding that symptoms are experienced in everyday life is just a function of modernity, this is not the case, with another study finding that all participants belonging to indigenous groups living in a remote area of the Philippines had experienced symptoms in the last thirty days (245). This pattern of findings is not exclusive to adults. One study, using parental-report of symptoms, indicated that 56% children aged three to five years experienced at least one symptom in the last fourteen days (246).

There is evidence that misattribution of commonly occurring symptoms may underlie many of the symptoms that are attributed to certain exposures. A recent comprehensive systematic review investigating the nocebo effect found that symptom misattribution was a key factor underlying the nocebo response (220). Misattribution of symptoms can occur after exposure to both active and inert substances. For example, in Auckland, a number of residential and industrial areas were sprayed using a biological insecticide to eradicate a moth which posed a threat to local flora and fauna (247, 248). People who lived in the spray zone completed questionnaires ten weeks before aerial spraying of the insecticide began which included the number of symptoms experienced in the past four

weeks. After the area had been sprayed three times, participants completed a follow-up questionnaire. The number of symptoms that people reported following the insecticide spray was strongly associated with the number of symptoms reported before spraying. However, this result should be taken with caution as when using a Bonferroni correction to account for multiple comparisons, this association was no longer significant. Participants were also asked whether their symptoms could be attributed to the insecticide spray; an association between the number of symptoms attributed to the spray and baseline symptom reporting was found (248).

Another study investigated the number of symptoms experienced by adults receiving a travel vaccination (249). Prior to receiving the travel vaccination, participants were asked whether they had experienced any symptoms in the past four weeks. Twenty minutes and one week after vaccination, participants were asked to indicate if they had experienced any symptoms 'since [their] vaccination' and whether they attributed the symptoms to the vaccine. Participants who were symptomatic before vaccination reported more symptoms twenty minutes after vaccination and attributed more symptoms to the vaccine than those who were not symptomatic. There was no association between pre-vaccination symptoms and post-vaccination symptom experience or symptom attribution one week after vaccination. Taken together, evidence suggests that the symptoms commonly experienced in everyday life are sometimes mistakenly attributed to a new exposure. This effect may be particularly prevalent in measures of symptoms immediately following exposure.

3.2.2 Expectation

There are two key lines of evidence which support the role of expectations in the perception of symptoms. First, it has been demonstrated numerous times that expectations influence perception of symptoms in different clinical populations. For example, expectations of nausea before chemotherapy have also been strongly associated with experiencing nausea during chemotherapy (250), even when controlling for other pharmacological and physiological predictors of nausea (251), and most recent experience with chemotherapy (252). Asthma patients who expect to experience more symptoms of asthma are also more likely to perceive symptoms (236). A systematic review of psychological predictors of

neck and back pain in adults has also found that expectation of pain was associated with later perception of pain (253).

Second, laboratory studies with healthy volunteers have shown that experimentally induced expectations drive symptom perception. One recent systematic review of factors associated with the nocebo effect identified seventy experimental studies and nineteen prospective studies (220). Results indicated that baseline expectation, verbal suggestions of symptoms, learning from previous experience and seeing another person experiencing symptoms following exposure were key predictors of the nocebo response (220). Expectation was also identified as a key component in the perception of non-specific side-effects from medication in another systematic review (219). Overall, the evidence for the importance of expectations is robust.

3.2.2.1 *Verbal suggestion of symptoms*

Expectations do not simply appear. Several triggers for expectations have been explored. Perhaps the most researched of these is the verbal suggestion of symptoms. The effect of a verbal suggestion of symptoms can be strong, overriding the true pharmacological action of a drug. For example, one study manipulated instructions about the effect of a drug, with participants receiving no information about the drug, being given information that the drug was a relaxant, or being told that the drug was a stimulant (254). In the active drug group, participants received carisoprodol, a muscular relaxant drug which causes drowsiness, while in the sham group participants received lactose pills. Regardless of whether they were given the active drug or the sham pill, participants who received information that the drug was a stimulant showed increased feelings of tension.

Expectations related to the intensity of symptoms can also influence their perceived severity. One study, investigating perceived pain and cortical activation in response to an infrared laser, gave participants a valid or invalid auditory cue about the pain intensity of upcoming laser stimuli (255). Participants' pain perception was influenced by the auditory cue rather than the intensity of the stimulus, with more intense stimuli which were preceded by low intensity pain cues being rated as less painful, and less intense stimuli preceded by high

intensity pain cues being rated as more painful. Neuroimaging techniques indicated that invalid cues might modulate pain experience through amplification of the nociceptive response in early cortical processes. However, results should be taken with caution as only six participants were included in the study.

Other evidence for the influence of symptom expectation on later symptom perception comes from clinical trials showing similar rates of adverse effects in the placebo and active drug arms. As noted earlier (Chapter 3, paragraph 2 and 3), similar prevalence and patterns of side-effects in the placebo and active drug arms are reported in clinical trials for anti-migraine medications (214), anti-depressants (215), statins (210) as well as the child influenza vaccine (78). Expectations are likely to arise from the information about the medications given to participants prior to the blinded portion of the study (214, 215). Researchers' framing of the medication will influence participants' expectations of the incidence of adverse effects. Thus, both participant and researcher expectations may influence later symptom perception.

Health professionals are not the only source of information which may influence expectations about symptoms. Information about individual symptoms and symptom likelihood from different sources, such as friends or family, the media and other official sources may also influence expectations (236). In New Zealand, in the month following news coverage of the reformulation of tablets for thyroid hormone replacement treatment, there was an increase in side-effect reporting even though there was no change to the active ingredient in the tablet (256). In particular, reports of symptoms explicitly mentioned in individual news stories increased significantly. Also in New Zealand, a retrospective longitudinal study investigating adverse event reporting for the HPV vaccination in relation to Google searches and news coverage found that the number of Google searches in the current month was associated with adverse event reporting (257). Negative media coverage in the previous month was associated with the number of adverse events reported. Furthermore, the effect of news coverage in the previous month on adverse event reporting was partially mediated by Google searches in the current month.

People may judge information from individual sources based on their trust in that source. For example, in a nationally representative survey of American adults, physicians were rated the most trusted source of health information, followed by the internet, television, family or friends, magazines, newspapers and radio (258). However, peoples' trust in a source does not necessarily mean that they would consult that source for health advice in the first instance. Although 49.5% of people indicated that they would go to their physician first for advice, 48.6% people consulted the internet as their first source of information, with only 10.9% consulting their physician first. Similarly, another study asking parents of children aged less than one year about their trust in sources of information about the MMR vaccine and outbreak found that while information from government sources and healthcare practitioners was the most trusted, online and television news and social media were the most used sources of information (259). It is likely that ease of access to information plays an important part in influencing one's choice of source of information to consult. Thus, peoples' expectations of symptoms may be influenced by multiple sources.

3.2.2.2 *Observation of symptoms in others*

Fewer studies have investigated the social modelling of symptoms, in other words, the effect of seeing others undergo an exposure which brings about symptoms. Where studies do exist, they investigate the effect of social modelling on the nocebo response to inert exposures only, presumably due to ethical considerations. The effects of social modelling can be strong, with some studies indicating that social modelling of symptoms can bring about changes in physiological outcomes. One study exposed participants to a female confederate who stated that she either felt 'calmer and more relaxed, and like [her] heart rate [had] gone down' (social modelling condition) or that she '[didn't] feel any different' (control condition) after having supposedly taken a fast-acting beta-blocker (260). After having taken an inert pill, participants in the social modelling condition had decreased heart rate, blood pressure and anxiety; these effects were not seen in participants in the control condition.

While social modelling of symptoms has been identified as one of the strongest predictors of the nocebo effect in a recent systematic review of eighty-nine studies (220), there is some evidence that this effect may be more prominent in

females than in males (261, 262). Faasse and colleagues have conducted two studies in which participants were randomised to view either a study confederate modelling the adverse effects of a pill (social modelling condition) or 'not feeling any different' (control condition) (261, 262). The first study used a female confederate to model the adverse effects of the pill (261). Social modelling influenced the physiological marker of blood pressure, with participants in the control condition showing larger decreases in blood pressure after taking the inert pill compared to those in the social modelling condition; there was no effect on heart rate. While the positive and desired effects of the inert pill were experienced by male and female participants, social modelling of adverse effects by the female confederate only increased female participants' reports of side-effects. The second study used both female and male confederates to model the adverse effects of the pill, finding that participants (both male and female) who witnessed the confederate experiencing adverse symptoms perceived more specific adverse symptoms of the medication during the experimental session; female participants reported more general symptoms during the session than male participants regardless of the modelling condition (262). At a 24-hour follow-up, as well as specific adverse symptoms, participants who had seen the confederate modelling symptoms reported more general symptoms and misattributed more symptoms to the inert pill.

3.2.2.3 *Prior learning*

Another mechanism which may influence expectations is learning from previous experiences. Learning that symptoms are associated with an exposure may lead to the conditioned experience of symptoms when later presented with that same exposure. While some theories suggest that expectancy and conditioning are separate mechanisms which cause symptoms as part of the nocebo response (263), it is likely that learning feeds into expectations. As well as being associated with the nocebo response (220), prior learning that an exposure causes symptoms has also been implicated in the perception of medically unexplained symptoms (234) and non-specific symptoms attributed to medication (219). Prior learning may also underlie some of the adverse events experienced by participants in the placebo arm of randomised-controlled trials (215). The effect of learning that a medication causes side-effects has been investigated in a group of participants

taking the antidepressant amitriptyline (264). Participants were randomised to either the active medication group (amitriptyline), or the placebo group, in which participants received placebo pills which appeared identical to the active drug. Participants were instructed to take the pills each night alongside a neutral stimulus, a lychee flavoured drink. Participants randomised to the active medication group took amitriptyline for four nights, followed by a three-day washout period. After the four-night acquisition phase, participants taking amitriptyline reported more anti-depressant specific symptoms than those taking the placebo pill; there was no difference between groups for non-specific side-effects. On the eighth day, all participants were given a placebo pill alongside the lychee flavoured drink. Participants assigned to the active medication group reported more anti-depressant specific symptoms than those taking the placebo pill.

3.2.3 Beliefs and attitudes about medicines and other technologies

There are subtle differences between beliefs and attitudes. Beliefs have been defined as 'the probability dimension of a concept' (265) (p. 35), while attitudes are the 'evaluative dimension of the concept' (265) (p. 35). Thus, beliefs encompass the likelihood of something happening, whereas attitudes encompass the tendency to consistently evaluate a particular entity in a negative or positive manner (266). Beliefs and attitudes have also been implicated in the nocebo response, and are thought to manifest through expectation or changes in attribution of symptoms (220). In the case of the child influenza vaccine, parents' beliefs about medicines, perceptions of how sensitive their child is to medications, modern health worries and general attitudes may be important.

3.2.3.1 *Beliefs about medicines*

Beliefs about medicines, in particular beliefs about their necessity and concerns associated with their use, have been consistently associated with medication adherence in a range of conditions including asthma, chronic pain from dialysis, diabetes, HIV, back problems and other chronic illnesses (267). While the association between beliefs and symptom perception is less well documented, negative medication beliefs are associated with perception of side-effects from medication in patients with rheumatoid arthritis (268) and asthma (269).

Beliefs about medicines have also been investigated more generally, focussing on the notions that medicines cause harm and are overused. Vaccination refusal has been associated with the notion that vaccines cause harm through adverse effects (91, 95, 270) as well as that vaccines are overused, playing into perceptions that vaccination will overburden the child's immune system (93). While these beliefs have been consistently linked to vaccination uptake, less research exists investigating their impact on perception of symptoms. Where evidence does exist, it is mixed. Among heart failure patients, the perception that medicines were overused was associated with perceiving at least one side-effect from medication for heart failure in the past four weeks; no association was found between perceived harm and perception of side-effects (271). Although not investigating symptom perception itself, in a nationally representative sample of English adults, those who believed that medicines were more harmful and were overused had higher expectations of side-effects from a hypothetical medication for dizziness and kidney failure (272).

A further two studies have investigated the role of beliefs about medicines with relation to a hypothetical new asthma drug 'molair' (273, 274). In these studies, participants were given variants of an information leaflet to read, in which headache was not mentioned as a side-effect of 'molair.' Participants were asked to imagine they had been taking the new drug daily for the last two weeks with no symptoms, but had begun to develop a headache at the beginning of the third week. Participants were then asked whether the headache had been a symptom of 'molair.' Symptom misattribution to 'molair' was associated with general and specific negative medication beliefs (273, 274). However, when specific medication beliefs about the necessity of 'molair' and concern surrounding it were controlled for, the association between general beliefs about medicines and symptom misattribution was no longer significant (273). Participants were later presented with a list of side-effects, some of which were listed in the patient information leaflet for 'molair' (274). Participants who thought medicines were more harmful in general were less able to correctly identify whether individual side-effects had been listed in the leaflet and recalled fewer side-effects correctly.

3.2.3.2 *Perceived sensitivity to medicines*

Perceived sensitivity to medicines is associated with symptom perception in everyday life. In a nationally representative sample of the New Zealand adult population, perceived sensitivity to medicines was associated with the number of symptoms experienced over the last week (275). When split into groups with low, moderate and high perceived sensitivity to medicines, post-hoc analyses indicated that there was no difference in symptom reporting in those with low and moderate perceived sensitivity to medicines, while those with high perceived sensitivity to medicines perceived more symptoms in the last seven days than both low and moderate groups. However, these analyses were not adjusted for demographic characteristics despite associations being found between higher perceived sensitivity to medicines and being female, unemployed and older.

Perceived sensitivity to medicines may also influence perception of symptoms after taking medication. Perceived sensitivity to medicines was associated with the number of symptoms reported and symptom attribution to a travel vaccine, twenty minutes after vaccination (249, 276). One week after vaccination, only the number of symptoms reported was associated with perceived sensitivity. In people starting antiretroviral therapy, perceived sensitivity to medicines was associated with perception of side-effects after one month of treatment (277).

Reactions to hypothetical medications for dizziness and kidney failure were also investigated with relation to perceived sensitivity to medicines, with those who thought they were more sensitive to medicines having higher expectations of side-effects (272). In response to a fictitious asthma medication however, no association was found between perceived sensitivity to medicines and misattribution of headache to ‘molair’ when controlling for demographic characteristics and beliefs about medicines (273).

3.2.3.3 *Modern Health Worries*

Concerns about aspects of modern life, such as potential toxic interventions (including vaccination programmes), environmental pollution, tainted food and radiation, and their impact on health are associated with increased symptom reporting in everyday life. This association has been found in a cohort of New Zealand students (278), North American students (279), young adults in Hungary

(280), and the general population aged fourteen and above in Germany (281). There may be some specificity in associations between the different aspects of modern health worries and symptom reporting. For example, those with higher concerns about tainted foods had increased gastrointestinal symptoms, while those who were more worried about toxic interventions (including vaccines) reported more musculoskeletal pain (278).

Modern health worries are also associated with symptom perception following exposure to potential health threats. For example, participants who scored more highly for modern health worries attributed more symptoms to a recent aerial spraying of crops with pesticide (247, 248).

Other potential modern health worries such as hazardous waste sites, high voltage transmission lines and emissions from industry have also been investigated. For example, although there was no direct association between perceiving odours from a biofuel facility and symptom perception, there was an indirect association mediated by perceived pollution and health threats (282). Participants who thought a hazardous disposal waste site was having an effect on their environment were more likely to perceive symptoms than those who did not (283), as were participants who exhibited more environmental worry (284). Industry-related worries was also associated with symptom in people living close to heavy industry such as coking works and steel and petrochemical complexes (285). Worry about transmission lines was associated with reporting more health problems in participants who lived close to high voltage transmission lines in the USA (286).

3.2.3.4 *General beliefs and attitudes*

General beliefs and attitudes about illness and recommended illness prevention methods may also influence subjective perception of symptoms. One recent study asked whether students had ‘ever had adverse reactions after being vaccinated’ (287). Students who reported moderate or severe vaccine side-effects, compared to those who had not experienced side-effects or in whom side-effects were mild, were more likely to have a fear of side-effects and associate the term ‘vaccination’ with needles and syringes. Beliefs about symptoms and illness may lead to the perception of symptoms. For example, patients with medically

unexplained symptoms and those with hypochondriasis tend to hold the inaccurate belief that all bodily sensations and symptoms are a sign of illness (288, 289).

3.2.4 Psychological traits

Traits can be defined as ‘dimensions of individual differences in tendencies to show consistent patterns of thoughts, feelings, and actions’ (290) (p. 25). Psychological traits, such as positive and negative affect, pessimism and neuroticism have been implicated in the nocebo response (220). Several convergent lines of evidence support the notion that psychological traits influence symptom perception. Anxiety and negative affect cause heightened attention towards bodily sensations and lower the threshold at which sensations are detected (231, 238) and it is likely that other psychological traits may influence symptom perception through similar mechanisms. Negative affect and neuroticism are also thought to bring about symptom reporting through increased scanning for, perception of, reaction to and complaints about, physical sensations (239, 240).

There is much overlap between psychological traits (291, 292), with similarities being identified between dispositional optimism, pessimism, neuroticism and negative affect (293, 294). However, despite substantial overlap between psychological traits, there is evidence that separate traits measure distinct dimensions (295). The role of anxiety, positive and negative affect, neuroticism, and optimism and pessimism in symptom perception is explored.

3.2.4.1 *Anxiety*

Although anxiety has long been associated with the nocebo effect (219), a recent comprehensive review found weak evidence for an association with state and trait anxiety (220). A study investigating symptom misattribution in response to a hypothetical new asthma drug also found no association between state or trait anxiety and symptom misattribution (273).

The role of anxiety seems to be stronger in functional syndromes, with a meta-analysis finding that patients with three of four functional syndromes (irritable bowel syndrome, nonulcer dyspepsia and chronic fatigue syndrome; not fibromyalgia) were more anxious than healthy controls (238). There was also

some evidence that those who were more anxious experienced a higher number of medically unexplained symptoms (238). However, it is difficult to uncover the direction of this relationship. The association between anxiety and symptom perception in somatisation persists across cultures, with one study finding that after adjusting for the effects of age and sex, those identified as somatic by the Somatic Symptom Index, were more likely to have concurrent generalised anxiety disorder, as diagnosed by ICD-10, in twelve sites across eleven countries (296). Associations between generalised anxiety disorder and the more restrictive ICD-10 diagnosis of somatisation disorder were not investigated. There is also evidence for an association between anxiety and symptom perception in general healthcare, with anxiety being a strong predictor of symptom reporting in patients in primary care in the USA (297).

Worry about symptoms may also play an instrumental part in symptom perception. For example, patients with somatisation display increased illness worries (234). In patients with chronic fatigue syndrome and multiple sclerosis, worry was associated with making somatic attributions for symptoms (298). In a six-day diary study of secondary school Dutch teachers, worry frequency and duration were associated with number of symptoms experienced, when controlling for number of symptoms experienced the previous day (299). When investigating worry intensity, only worry intensity remained associated with the number of symptoms reported; worry frequency and duration were no longer associated.

3.2.4.2 *Negative Affect*

Trait negative affect is consistently correlated with symptom report (240). A diary study in which participants were asked to complete a questionnaire every six hours while they were awake, found that participants with higher levels of negative affect were more likely to report somatic symptoms (300). The study also investigated variations of affect within-participants, finding that both increased negative affect and decreased positive affect were associated with reporting more somatic symptoms. Increased negative affect has also been associated with symptom reporting following an exposure, such as receiving a travel vaccination. For example, participants with increased negative affect

reported more symptoms one week after the vaccination and attributed more symptoms to the vaccination (249).

Among participants presenting to primary care practices, those with increased negative affect and decreased positive affect reported a higher number of medically unexplained symptoms (301). Patients in primary care with medically unexplained symptoms who had high positive affect were more likely to report a decrease in the number of symptoms experienced at a six-month follow-up (302).

3.2.4.3 *Neuroticism*

Less research exists investigating the role of neuroticism on symptom reporting. In a nationally representative sample of American twenty-four to seventy-four year olds without self-reported medical problems, neuroticism was associated with perceived poor health (303).

There is mixed evidence for an association between neuroticism and medically unexplained symptoms, with one study finding that patients with medically unexplained symptoms show elevated neuroticism (304). Another study found no association between neuroticism and medically unexplained symptoms in adults presenting to primary care when controlling for positive and negative affect (301, 302).

3.2.4.4 *Optimism and pessimism*

Very few studies have investigated the role of optimism and pessimism in subjective symptom perception. Where evidence exists, it yields mixed results. Patients with the functional syndrome ‘temporo-mandibular dysfunction’ who were less optimistic showed a lower pain tolerance than more optimistic patients and healthy controls (305).

Pessimism was associated with symptom perception in undergraduates who were told they were taking an over-the-counter pill which caused unpleasant symptoms (306). However, there was no association in a group who were unsure whether they were taking an inert placebo pill or the active medication or in the control group who were told they would be taking an inert pill (306).

3.2.4.5 *Other personality traits*

Depression has been investigated in relation to symptom perception in many studies. A systematic review identified that depressed mood increased the risk of neck and back pain in adults (253). Another systematic review of psychological factors associated with chronicity of back pain also identified distress and depressive mood as contributors, however these results should be taken with caution as few studies were included in the review (307). Associations between clinical depression and somatisation disorder have been found across different cultures, with one study finding an association in fourteen sites across thirteen countries (296). Depression was also a strong predictor of symptom reporting in patients in primary care in the USA (297). An experimental study manipulating mood found that college students with influenza or the common cold who underwent mood induction to a sad mood state reported more aches and pains than those inducted to a happy mood state (308). However, not all studies investigating symptom perception and depression have found an association. Depressive symptoms in adolescents were not associated with self-reported everyday symptom perception two years later (309).

Other studies have investigated the grouped effect of multiple psychological traits on symptom perception. A systematic review reported that of eleven studies included which investigated stress, distress or anxiety, all found an association with neck and back pain (253). One study, investigating patients who presented at primary care services with medically unexplained symptoms, grouped negative affect, anxiety and depression scores to give a composite measure of 'negative affect,' which was associated with consistently reporting high levels of medically unexplained symptoms (302).

3.2.5 Cognitive processes

Attention and interpretation play a central role in many models of symptom perception (233). However, they tend to be discussed in terms of the attention one pays to bodily sensations, and the interpretation of the cause of symptoms, also known as symptom attribution. While the role of biases in information processing has been researched less, cognitive biases of attention and interpretation may also influence subjective symptom perception.

3.2.5.1 *Attention*

Although attention to one's own bodily sensations allows identification of injuries, increased attention to bodily sensations is associated with increased symptom reports (234). For example, increased body consciousness in healthy participants was associated with making somatic attributions for a bodily sensation (310) and with increased symptom reporting in everyday life (311). Patients with somatisation syndrome and those with hypochondriasis also show increased body scanning (288). Further evidence that symptom report may be associated with increased attention to subjective bodily sensations comes from research finding that when distracted by a mental arithmetic task, patients with psychosomatic diseases showed decreased pain intensity and pain unpleasantness (312).

It could be hypothesised that people who pay more attention to their bodily sensations are more able to detect physiological sensations, however this is not the case. Patients with hypochondriasis often consider themselves to be more sensitive to harmless bodily sensations, however, they show no increase compared to healthy controls in their ability to detect tactile stimuli (313).

Despite evidence indicating that patients with functional syndromes display increased attention to bodily sensations, evidence for the role of attention bias in perception of medically unexplained symptoms is inconclusive (234). Meta-analytic results indicate that although chronic pain patients display attention biases towards pain-related stimuli, they do so no more than healthy controls (314). Chronic fatigue patients display attention biases only when using particular tasks (315-318). One explanation for this pattern of results may be that chronic fatigue patients are only biased in the elaborative phase of attention, in which patients relate a word to their personal concerns, rather than the orientation phase of attention, in which participants direct their attention (318). Similarly, in somatoform patients, bias for physical threat words was found at the supraliminal but not subliminal level, suggesting that somatoform disorders may be associated with maladaptive biases in later stages of processing, such as interpretation (319). Results for irritable bowel syndrome patients are mixed. One study found that compared to controls, who oriented more quickly to neutral words than pain words, irritable bowel syndrome patients showed no difference in their

orientation to pain and neutral words (320). Another study found that differences in attention bias between irritable bowel syndrome patients and healthy controls existed for socially threatening words (321). Taken together, it seems that while patients with functional syndromes may display attention biases, these biases are displayed only in the more conscious, rather than unconscious, phases of information processing.

Content-specific attention biases have been found in patient populations with physical illnesses such as asthma (208), a history of cancer (322), a family history of cancer (though who have never had the disease themselves) (323) and pathological health anxiety (324). Those who have experienced a minor health-related problem in the last month, but who are otherwise generally healthy, and those with poorer self-assessed health also systematically attend to health-related and illness-related words compared to non-illness or neutral words (325, 326). Although studies are cross-sectional and causation cannot be inferred, studies seem to indicate that a history of symptoms is associated with greater attention to symptom-related stimuli. Thus, symptom experience may influence bias, rather than bias influencing symptom experience.

3.2.5.2 *Interpretation*

Less research exists investigating the interpretation of bodily sensations as symptoms. Interpretations are likely to be made in line with schema already held by the individual, with people selectively searching for confirmatory sensory information and forming interpretations which agree with their hypotheses (327). For example, one study found that groups with diagnoses for different psychological disorders held different interpretations of the cause of their symptoms, in line with relevant schema (328). In this study, participants with anxiety disorders tended to believe that bodily sensations were a result of their anxiety, giving more psychological interpretations of symptoms, whereas those with hypochondriasis tended to hold more somatic interpretations of bodily sensations, interpreting bodily sensations as symptoms of illness (328).

Increased health anxiety can impact symptom interpretation even in non-clinical populations. Healthy participants with increased health anxiety tended to interpret diagnostic information about whether they were at risk for experiencing problems

during painful medical tests more negatively than those with lower anxiety (329). More anxious individuals also tended to catastrophise more about the meaning and implications of bodily sensations experienced (329).

Although these studies show that those with specific disorders tend to interpret the cause of symptoms according to their own schema, they do not measure whether systematic interpretation biases differ in those who perceive more physical symptoms. While few studies have investigated the associations between interpretation bias and symptom perception in functional syndromes, results indicate evidence for an association. A systematic review and meta-analysis of the role of interpretation bias in chronic pain found that when presented with ambiguous words, participants with chronic pain tended to choose the pain-related or illness-related interpretation (330). A recent systematic review found that chronic fatigue patients showed negative interpretation biases on tasks where they had time to generate their responses, but not when having to make more automatic, spontaneous responses (318). Again, this points to the notion that biases in chronic fatigue patients may only manifest in the elaborative phase of information processing, when patients have the time to draw upon existing illness schemas. While causation cannot be inferred, evidence suggests that negative interpretation biases underlie perception of symptoms in functional syndromes.

3.2.6 Personal characteristics

Higher rates of symptoms are consistently perceived by females than males in health surveys, clinical registration of health complaints by physicians, and studies investigating symptom reporting (331). In the primary care setting, female sex was associated with increased symptom reporting (297) and reporting high levels of medically unexplained symptoms (302). Female sex was also associated with number of self-reported physical symptoms in a population of adolescents attending school (309). Higher side-effect reporting in females than males has also been found for corticosteroid drugs for asthma (269). Gender effects in the nocebo phenomenon are less clear. Though most research points to an association between female sex and symptom perception, a meta-analysis identifying factors associated with the nocebo response in placebo-controlled clinical trials for neuropathic pain (pain which arises as the result of a lesion or disease affecting the somatosensory system) found an association between male sex and the

nocebo response (332). More recently, a comprehensive systematic review of factors associated with the nocebo response found no significant gender effects (220).

Sex differences in symptom perception, in particular perception of pain, have been investigated using neuroimaging techniques, finding differences in patterns of neural activation in response to pain (333). Females show increased activation in areas of the brain associated with affective and motivational components of pain, including emotion-arousal, compared to males (334, 335). It is therefore possible that differences in pain reporting are due to females placing more emotional importance on pain than men, rather than there being differences in sensory impulses in the central nervous system (334).

The direction of association between symptom perception and other personal characteristics is less clear. For example, age has been investigated by multiple studies with varying results. While not associated with full somatisation disorder, when using a less rigorous classification, participants aged forty-five and over were more likely to fall into the somatisation category than younger participants (296). In contrast, another study using primary care data indicated that younger participants reported more symptoms (297). Younger participants were also more likely to misattribute symptoms to the fictitious drug ‘molair’ (273). Education and socio-economic status were also investigated with relation to symptom reporting in primary care, finding that patients with lower education and socio-economic status reported more physical symptoms (297).

3.2.7 Clinical characteristics

Clinical characteristics may also impact subjective symptom perception. The number of medical comorbidities was associated with increased symptom reporting in primary care patients in the USA (297). This is logical, with those who have more comorbidities, likely experiencing more symptoms.

Other studies have investigated self-reported symptom perception in children of parents with chronic illnesses. A recent meta-analysis investigating chronic pain found that children of parents with chronic pain were more likely to report chronic pain themselves (336). A longitudinal study following a birth cohort until adulthood found that children who experienced recurrent abdominal pain were

more likely to have parents who reported illness in their own childhood (337). In these cases, child-reported symptom perception could be due to biological factors, such as the child being more likely to inherit illness from their parents, or psychological factors, with children adopting similar coping strategies to their parents.

3.2.8 Interaction between factors

So far, factors associated with subjective symptom perception have been discussed individually. However, as proposed by models of symptom perception, it is likely that these factors interact with each other. Studies have focused on the potential mediating and moderating effects of psychological traits on symptom perception. For example, there is evidence that the relationship between neuroticism and symptom perception may be mediated by negative affect. This was the case in patients with medically unexplained symptoms (301) and Type 2 diabetes (239). Low positive affect also mediated the relationship between neuroticism and symptom perception in patients with medically unexplained symptoms (301). Negative affect has also been proposed to mediate the perception of asthma symptoms, as it explains more of the variance in asthma symptoms than does pulmonary function (338).

Neuroticism moderated the relationship between negative affect and symptom reporting in patients with Type 2 diabetes, with those who were low in neuroticism showing a stronger relationship between negative affect and symptom reporting (239). Neuroticism also moderated the relationship between positive affect and symptom reporting, with patients with high, but not low, neuroticism, displaying an association between positive affect and symptom reporting (239).

Beliefs, attitudes and personal characteristics may also interact with subjective symptom perception. For example, one study found that worry intensity mediated the relationship between stressful events and symptom reporting in Dutch teachers (299). Another study found that the relationship between modern health worries and somatic symptoms in adolescents was mediated by health anxiety and somatosensory amplification (280).

3.3 Parental perception of symptoms

There is strong evidence for the influence of psychological factors in subjective symptom perception in oneself, as well as numerous models which attempt to explain symptom perception both generally and across a range of medical conditions (233). There is much less research, and no models explaining how psychological and social factors may affect the perception of symptoms in someone other than oneself.

The ability to accurately identify symptoms in others is particularly important for parents. If parents are unable to accurately perceive symptoms in their child, they might incorrectly detect or miss signs of illness, symptoms of allergy or intolerance, or side-effects of medications, and make inappropriate decisions for their child regarding medical care, lifestyle, or medication adherence as a result. Perceived food intolerance is one example of this. Parents who perceive symptoms after their child eats a certain food may conclude that their child is intolerant. Approximately one-third of parents believe their child has a food sensitivity (339). However, the majority of these children do not undergo any formal testing of food allergy such as skin prick tests or oral food challenges. When formal testing does occur, the actual prevalence of food hypersensitivity is much lower (339, 340), suggesting that many parents are unnecessarily restricting their child's diet as a result of this misperception (341).

Parental perception of symptoms in children is common. Although formal data are scarce, one study based on parental report estimated that 56% of children aged three to five had experienced symptoms such as headache, stomach ache, tiredness and dizziness in the last fourteen days (246), a broadly similar rate to that seen in adults (241-243). While rates are similar, it is likely that different factors come into play when identifying symptoms in others and oneself. While perception of symptoms in oneself is driven by detection of internal cues and bodily sensation, parental perceptions of symptoms in a child relies on external cues, such as observations of the child's behaviour, or listening to and assessing self-report from the child. Parents of young or severely disabled children, who are unable to verbalise their bodily sensations, may have to rely solely on observation of the child's behaviour.

To collate the available evidence regarding factors affecting parental perception of symptoms, I conducted a systematic review to identify psychological and social factors pertaining to the parent and child which are associated with parent-report of physical symptoms in one's child.

3.4 Methods

I conducted a systematic review in accordance with PRISMA criteria (104), to identify factors associated with parental perception of symptoms in children. I searched Embase, Ovid and PsycINFO through OvidSP; and Scopus. The final search used the terms (Parent* ADJ3 (perception OR perceive)) AND (side effect OR symptom* OR pain* OR asthma*). Asthma was included in the search terms as it is a condition experienced commonly in childhood, which was prevalent in my preliminary searches. MeSH terms were also searched where possible. Databases were searched from inception to 12th July 2018. References and forward citations of included articles were also searched.

3.4.1 Inclusion criteria

I applied the following inclusion criteria:

Participants: Studies were included if they investigated parents of children aged zero to eighteen years. Studies were excluded if parents discussed symptom report outcome measures with their child or if it was unclear whether the parent or the child completed outcome measures.

Predictors/Exposures: Studies were included if they investigated the association between psychological or social factors and parental perception of symptoms.

Outcomes: Studies were included if the outcome was parental report of symptoms in the child, including pain, asthmatic symptoms, side-effects from medication, or perceived allergy or food intolerance. Outcomes relating to parental contact with health professionals following symptom perception were excluded. Outcomes based on parental report of a diagnosis by a healthcare practitioner for the child were also excluded.

Study reporting: Only studies published in English were included.

3.4.2 Data extraction

I extracted information about study design, inclusion criteria, number of participants, child age, symptom type, symptom measure used, and predictors of symptom perception.

3.4.3 Risk of bias

I measured risk of bias using an amended version of the Downs & Black checklist (105), as in Chapter 2. This version did not include items referring to interventions as they were not relevant for any included study. The Downs & Black checklist has been validated (107) and is suitable for use in systematic reviews (106). The amended Downs & Black checklist included ten items assessing study reporting, two items assessing external validity, three items assessing internal validity (bias), three items assessing confounding (selection bias), and one item assessing whether there was a justification for the sample size used (power). I rated studies as good quality if they scored sixteen or over, moderate quality if they scored eleven to fifteen, and poor quality if they scored ten or less. I rated studies as scoring poorly if they: scored six or under out of a possible ten for study reporting; scored one or under out of a possible three for internal validity (bias) and confounding (selection bias); scored one or under out of a possible two for external validity; and if they did not include a justification for the sample size used.

3.4.4 Procedure

I developed the search terms, carried out the search, screened papers, extracted data and completed risk of bias assessment with guidance from GJR.

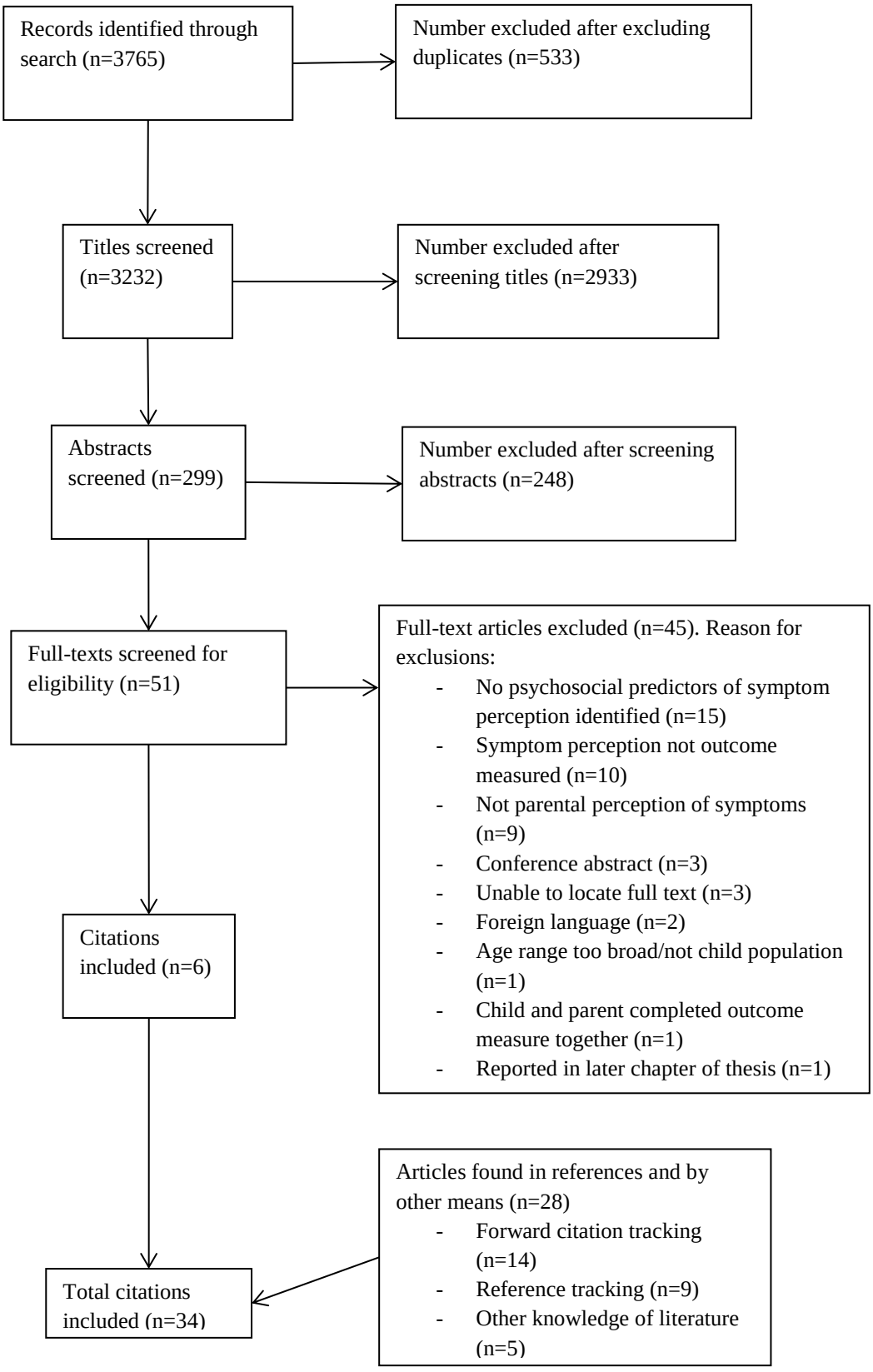
3.5 **Results**

3.5.1 Study characteristics

3765 citations were found by the original search. After removing duplicates, 3232 citations remained. After title, abstract and full-text screening, seven citations remained. This number included the paper that resulted from the cross-sectional study reported in Chapter 5. This study has been left in the search flowchart, but the study itself has been excluded from the results section of this review. Instead, its methods, results and contribution to the literature are reported in detail in

Chapter 5. Reference searching and forward citation tracking identified a further twenty-nine citations which met the inclusion criteria. Forward citation tracking identified the paper that resulted from the prospective cohort study in Chapter 6; this study has also been excluded from the current review, for the same reasons outlined above. This study is not included in the search flowchart. Thus, a total of thirty-four citations (six from the search and twenty-eight from reference searching and forward-citation tracking) reporting on thirty-two studies were included in this review (see Figure 4). Twenty-two studies used a cross-sectional design, seven used a cohort design and three used case-control design (see Appendix 3). Nine studies investigated somatic symptoms in general, with a further nine investigating solely headache, three investigating abdominal pain or stomach ache, and two investigating both headache and stomach ache; one investigated recurrent symptoms. Six studies investigated pain. One study investigated perceived food allergy and one investigated infectious diseases.

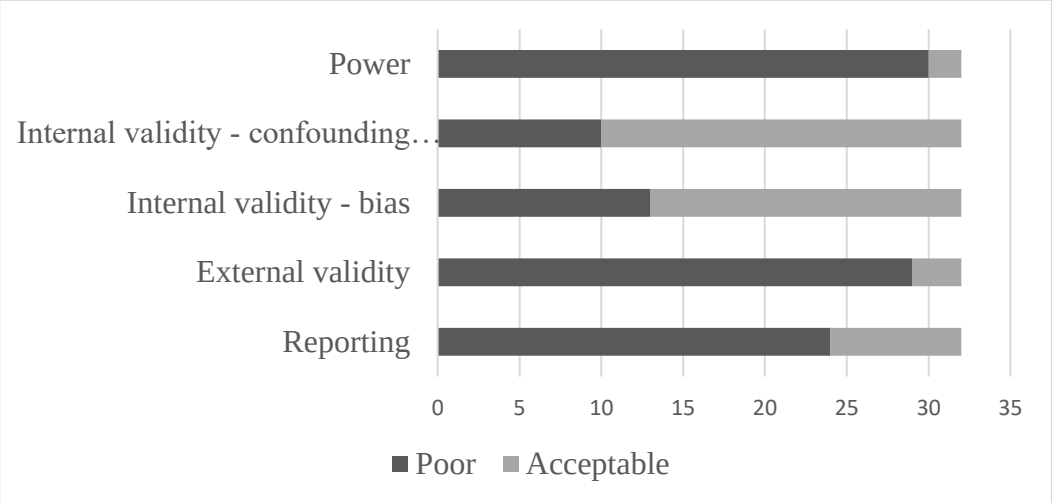
Figure 4. Flowchart depicting the selection of studies included in the systematic review of parental perception of symptoms with reasons for exclusion



3.5.2 Risk of bias

Scores ranged between three and sixteen out of a possible nineteen, with a median score of nine (see Appendix 3). There was only one good quality study (342). The majority of studies were poor quality (n=19), with twelve moderate quality studies. Only two studies gave a justification for the sample size used (343, 344) (see Figure 5). With respect to internal validity, ten studies scored poorly for confounding (selection bias) (345-354) and thirteen scored poorly for bias (246, 345, 346, 348-351, 353-358). External validity was poor in twenty-nine studies (246, 343-356, 358-373), while reporting was poor in twenty-four studies (246, 343, 345-349, 351-365, 369, 374).

Figure 5. Chart indicating number of studies included in the systematic review of factors associated with parental perception of symptoms displaying different aspects of risk of bias



3.5.3 Predictors of parental symptom perception

Parental and child psychosocial factors associated with parental perception of symptoms are reported in Table 5 (for full results tables see Appendix 4). Where studies used adjusted analyses only these are reported. Many studies used the Strengths and Difficulties Questionnaire (375), which is made up of five components: emotional problems, conduct problems, hyperactivity-inattention, peer problems and prosocial behaviour. Where possible I have reported results for each component separately.

3.5.3.1 *Parent psychosocial characteristics*

There was good evidence for an association between parent anxiety and parental symptom perception. One moderate quality study found an association between parent anxiety and report of somatic symptoms (373). Four studies found mixed evidence of an association with increased symptom presence, frequency and severity: two studies were moderate quality (367, 370-372) and two were poor quality (352, 353).

There was mixed evidence for an association between parent depression and parental symptom perception. Maternal depression was associated with perception of recurrent symptoms in one poor quality study (358), while a moderate quality study found mixed evidence (370-372). Three further studies, two moderate quality (364, 373) and one poor quality (354), found no association between increased presence and frequency of parent-reported symptoms.

There was mixed evidence for an association between parent distress or stress and parental symptom perception. Distress was associated with perception and frequency of parent-reported symptoms in a moderate quality study (374) and a poor quality study (246). Three moderate quality studies investigated the association between parental stress and perception and frequency of parent-reported symptoms. One found an association (373), one found mixed evidence for an association (366), and one found no association (361).

There was little evidence for an association between perceived emotional and social support and parental symptom perception. A moderate quality study found that paternal, but not maternal, low emotional support was associated with perception of recurrent stomach aches in the child (366). A poor quality study found an association between maternal relationship dissatisfaction and perception of a number of parent-reported symptoms (365). Conversely, a poor quality study found an association between high perceived emotional support and increased perception of concurrent headaches and stomach aches in the child (356). Two poor quality studies found no association with parental perception of recurrent headaches and stomach aches (354, 358).

There was little evidence for an association between parenting style and parental symptom perception. A poor quality study found an association between maternal

involvement and parent-reported somatisation (349). Conversely, a moderate quality study found an association between punitive behaviours and less frequent perception of headaches in the child (368). No association was found between parenting style and pain sensitivity in another poor quality study (348).

Only one poor quality study investigated the effect of believing the symptom was common with respect to parental symptom perception, finding that parental perception that food allergy was common was associated with parental perception of food allergy in one's child (357).

Table 5. Parent and child psychosocial characteristics associated with parental perception of symptoms

Category	Parent characteristic		Child characteristic	
	Studies finding an association / studies finding mixed evidence	No association found	Studies finding an association / studies finding mixed evidence	No association found
Anxiety	(373) / (352, 353, 367, 370-372)		(246, 347, 350, 359, 368) / (346)	
Depression	(358) / (370-372)	(354, 364, 373)	(350, 362) /	(346, 359, 368)
Attention deficit and hyperactivity			(246, 342) / (370-372)	(346, 363, 368)
Other psychological disorders	(369)		(246) / (346)	(368)
Emotional problems			(342, 368) / (356, 370-372)	
Stress	(373) / (366)	(361)		
Mental distress	(246, 374) /			(347)
Stressful/adverse life event	/ (365)		(246, 347) /	(344, 361, 366)
Behavioural or conduct problems or disorder			(355, 356, 370-372) / (342, 354, 358)	(346, 363, 368)
Total strengths and difficulties			(342, 343, 368, 370-372, 374) /	
Poor temperament			(370-372) / (348, 349, 373)	
Problem relationship with peers			(342) /	(346, 368, 370-372)
Perceived lack of emotional or social support	(356) – inverse association (high support, more symptom perception). / (366)	(354, 358)		
Parenting style	/ (349, 368)	(348)		

3.5.3.2 *Child psychosocial characteristics*

There was good evidence for an association between child anxiety and parental symptom perception. Child anxiety was associated with increased presence, frequency and severity of parent-reported symptoms in two moderate quality studies (359, 368) and three poor quality studies (246, 347, 350). Another poor quality study found mixed evidence of an association with parent-reported somatic symptoms (346). All studies investigated parent-reported child anxiety, aside from two (350, 368), which investigated child-reported anxiety. One poor quality study found mixed evidence for an association between parental report that the child was 'fearful or anxious' and perception of recurrent symptoms (360).

There was little evidence for an association between child depression and parental symptom perception. An association was found between child depression and presence and severity of parent-reported symptoms in two poor quality studies (350, 362). Two moderate quality studies (359, 368) and one poor quality study (346) found no association between child depression and presence, frequency and severity of parent-reported symptoms. All studies investigated parental reports of depression, aside from two (350, 368), which investigated child-reported depression. Three studies investigated the effect of child anxiety and depression together, with one poor quality study finding an association between child-reported depression and anxiety and parent-reported child somatisation (350). Parent-reported anxiety and depression was not associated with parental perception of recurrent headache in one moderate quality (344) and one poor quality study (363).

There was good evidence for an association between child emotional problems and parental perception of symptoms. Associations were found with parent-reported frequent or severe headaches in one good quality (342) and one moderate quality study (368). There was mixed evidence for an association with presence and frequency of parent-reported symptoms in one moderate quality (370-372) and one poor quality study (356).

There was mixed evidence for an association between child attention-deficit hyperactivity disorder (ADHD) and parental symptom perception. Two studies

found an association between ADHD and presence, frequency and severity of parent-reported symptoms: one study was good quality (342) and one was poor quality (246). One moderate quality study found mixed evidence for an association with recurrent stomach ache (370-372). Three studies found no evidence for an association between ADHD and presence and frequency of parent-reported symptoms: one study was moderate quality (368) and two were poor quality (346, 363).

There was mixed evidence for associations between other child psychological disorders and parental symptom perception. Adjustment disorder was associated with perception of parent-reported physical symptoms in a poor quality study (246). There was mixed evidence for an association between social phobia and separation anxiety and parental perception of physical symptoms in a poor quality study, however when investigated as a predictor of frequent somatisation an association was found (346). Neither social phobia nor separation anxiety were associated with parent-reported frequent headache in a moderate quality study (368). There was no evidence for an association between oppositional defiant disorder and parent-reported presence or frequency of symptoms in a moderate quality (368) and poor quality study (346). Parent-reported somatic symptoms were not associated with dysthymia and alexithymia (345, 346), or severe mood dysregulation (346).

There was mixed evidence for an association between child conduct disorder and behavioural problems and parental perception of symptoms. Conduct problems were associated with parent-reported perception and frequency of symptoms in one moderate quality study (370-372); a good quality study found mixed evidence (342). Two studies found no association: one moderate quality (368) and one poor quality (346). Behavioural problems were associated with parental perception of headache and stomach ache in two poor quality studies (355, 356); there was mixed evidence in two poor quality studies (354, 358). One poor quality study found no association between parent-reported recurrent headache and aggressive behaviour (363).

There was good evidence for an association between total high difficulties on the Strengths and Difficulties questionnaire and parental symptom perception. Total

high difficulties was associated with parental perception of frequent child headaches in one good quality study (342) and two moderate quality studies (343, 368) and with parent-reported recurrent stomach aches and frequent pain in two moderate quality studies (370-372, 374).

There was some evidence for an association between child temperament and parental perception of symptoms, however studies varied in the aspects of temperament measured. One moderate quality study found that increased activity and lack of rhythmicity of eating were associated with parent-reported recurrent stomach ache (370-372). One moderate quality study found associations with parent-reported somatisation only for certain aspects of temperament (373). One poor quality study did not distinguish between aspects of temperament, finding that child temperament was associated with parent-reported pain, but only in children with a birth weight over 801 grams (348). Another poor quality study found an association between emotionality (but not shyness, sociability or activity) and parent-reported somatisation in full-term children; there was no association between any aspect of temperament in extremely-low birth weight children (349).

There was little evidence for an association between adverse or stressful life events and parent-reported physical symptoms, with two poor quality studies finding an association (246, 347). Three moderate quality studies investigating presence and frequency of parent-reported symptoms found no association (344, 361, 366).

There was little evidence for an association between problematic relationships with peers and parental perception of symptoms. One good quality study found an association between peer problems and parent-reported frequent or severe headaches (342). However, three studies investigating presence and frequency of parent-reported studies, two moderate quality (368, 370-372) and one poor quality (346), found no association.

3.6 Discussion

While mechanisms underlying symptom perception in oneself are more clearly understood, less research has explored factors associated with parental perception of symptoms in children. Studies included in my review were heterogeneous,

investigating parents of children of different ages and with different medical conditions, and were generally of poor quality. Evidence for factors was sometimes mixed and difficult to interpret. In addition, as diary methodologies were not used, parental report of symptoms may have been affected by factors such as recall bias and therefore may not have mapped exactly on to symptom perception. Above all, my review highlights the need for better quality research in this important and seemingly overlooked area.

This point notwithstanding, some factors appear to be associated with parental perception of symptoms. These can be grouped into two broad categories previously identified by others (376): psychological traits and behavioural difficulties. Looking first at psychological traits, there was good evidence for an association between child anxiety and parental symptom perception, but less evidence for a role of child depression, ADHD and emotional problems. This mirrors findings for parent psychological traits. This pattern of findings is perhaps unsurprising. One of the conditions necessary for the diagnosis of anxiety disorders in adults is the presence of physical symptoms (377). In children, presence of recurrent somatic symptoms is also one of the diagnostic criteria for generalised anxiety disorder (378). However, the presence of physical symptoms is not included in the diagnosis of other disorders such as ADHD (379) or depressive disorder, aside from disturbed sleep and diminished appetite (380).

How child behavioural difficulties, such as having problems with peers, may affect parental symptom perception is poorly understood. While all studies investigating child temperament in the review found an association with parent-reported symptoms, no rationale was given for investigating these factors. Studies were heterogeneous in the aspects of behaviour and temperament measured, making interpretation difficult. Physical symptoms are not implicated in conduct disorder (381), with the exception of measures of rhythmicity of sleeping and eating which are sometimes included in temperament (e.g. the Carey Infant Temperament Scale Revised (382)). The effects of temperament and behaviour on parental symptom perception likely manifest differently in different parent-child dyads. Children perceived as ‘difficult’ may verbally report more symptoms, leading to increased parental symptom perception. Children may also behave differently in the presence of their parents, leading to increased possibility

of symptom detection by parents. For example, children display more pain in the presence of a parent than a stranger (383). Better quality research is necessary to clarify the nature of, and reasons underlying, associations between temperament and parental symptom perception.

One important question to consider is whether parent and child psychosocial factors are associated with increased symptoms experienced by the child, or increased parental detection of symptoms, irrespective of the child's subjective experience. This distinction has already been identified as a concern in the literature (373) and it is likely that both mechanisms are relevant. Theories attempting to explain how parental anxiety may increase child symptom experience include that parents model illness behaviour which is then replicated by the child; that parents reinforce symptomatic behaviour; that the child may be genetically predisposed to respond to environmental stress through somatisation; and that perceiving anxiety or physical symptoms in the adult may cause the child to experience anxiety or stress, which in turn may manifest as physical symptoms in the child (367, 371-373). Anxious parents may also pay more attention to the child, leading them to detect more symptoms (367, 371-373).

The effect of some psychosocial factors on parental symptom perception were conspicuous by their absence from my review. In particular, no studies investigated the effect of expectation on parental symptom perception. Given the importance of expectation in the nocebo effect (220) and the wealth of evidence suggesting that expectation influences symptom perception in oneself (219, 220, 234, 255, 260-262, 384), it is surprising that no studies have investigated the influence of parental expectation on parent-reported symptoms. One possible explanation for this dearth of research is that studies have so far focused on finding factors associated with increases in symptoms experienced by the child, rather parental reporting of symptoms. However, regardless of a child's subjective experience, parental perception and recall of symptoms will influence their decision-making about medical treatments or potential lifestyle adjustments. Therefore, it is important to identify factors which may influence parental perception of symptoms.

Although no studies were included in the systematic review, it may be the case that parental cognitive biases are associated with perception of symptoms. There is very little evidence in this field, with research into cognitive biases typically focussing on oneself. However, parental interpretation biases have been implicated in symptom perception, with mothers of children with chronic abdominal pain tending to interpret ambiguous emotional facial expressions as pain (385). While causation cannot be inferred, it seems plausible that consistent negative interpretation of ambiguous illness-stimuli may lead parents to perceive symptoms in their child. For example, in the case of the child influenza vaccination, if the child sneezed in the hours following vaccination, parents with negative biases for man-made health threats may interpret this as a side-effect of vaccination, rather than as a sign that the child is currently cold.

There is some evidence that parental attention biases are associated with symptom perception, with studies finding that caregivers of chronic pain patients have biased attention towards painful faces (386, 387). Caregiver attention bias for pain-related stimuli was also associated with increased reporting of pain in the child (387). Attention biases may be more influential in parental perception of symptoms in the child than in perception of symptoms in oneself, due to the reliance on external cues to identify symptoms in the child. However, as with the association between attention bias and symptom perception in oneself, it is likely that parents of children with chronic pain attend more to behavioural pain cues as a result of their child's pain experience. There are no studies investigating whether parental attention or interpretation biases are associated with perception of side-effects following vaccination.

3.6.1 Limitations of studies included in the review

Most studies included in my review were poor quality. In particular, studies fell short on reporting and external validity. Studies were also heterogeneous with regard to their populations and statistical analyses, used inappropriate statistical tests or did not report the statistical tests used (354, 358), or had small samples (354, 358). Symptom perception was also defined differently by different studies, with some studies using higher thresholds for symptom perception than others. Studies included in the review used many different scales to measure the same

construct; this was particularly notable for temperament and behaviour (307) and made it difficult to compare results between studies.

3.6.2 Limitations of the review

Several limitations of my review should be considered. First, symptoms perceived by parents in this review were wide ranging, including pain, allergy and non-specific symptoms such as headache and stomach ache. I was unable to investigate whether predictive factors differed in relation to different symptoms.

Second, few studies investigated the same factors, meaning that my conclusions for some risk factors are based on limited results and should be treated with caution.

Third, it was notable that only seven citations were identified through my search strategy, with most citations being found through forward citation and reference tracking. As parental perception of child symptoms is rarely studied as a topic in its own right and has no specific, easily-searchable terminology, relevant data were difficult to find. I also did not search grey literature. It is likely that other studies investigating relevant risk factors exist, but I was unable to locate them.

Fourth, I restricted my search to psychosocial predictors of parental symptom perception. Other studies exist investigating personal and clinical factors such as breastfeeding (388-390), smoke exposure (391-395), exposure to indoor dampness and mould (396, 397), attending day care (398), and number of siblings (399) on parental symptom perception, particularly with relation to child asthma and allergic symptoms. A full model of parental symptom perception may need to account for these factors.

3.6.3 Conclusions

Despite poor quality and heterogeneous research, some factors stand out as being associated with parental perception of symptoms. In particular, parent and child anxiety are likely to be associated with parental symptom perception, as are child behavioural difficulties. However, mechanisms underlying the latter are unclear. Parent and child psychosocial factors may impact symptom perception through increasing child symptom experience, or parental detection of symptoms irrespective of child symptom experience. Increases in parental symptom

perception are likely brought about by a combination of these aspects. Some factors which are likely to influence parental perception of symptoms have not yet been investigated. First, the effect of expectation in parental symptom perception has not been researched, despite strong evidence indicating its key role in the nocebo phenomenon. Second, potential underlying associations between parental cognitive biases and symptom perception should be investigated. Better quality research is needed to more fully understand the impact of, and mechanisms through which, psychosocial factors influence parental perception of symptoms.

Chapter 4. Summary, research aims and hypotheses

Influenza is a serious illness which causes complications in many and presents a significant financial and clinical burden. Fortunately, vaccination can reduce these burdens. In my literature review, I found evidence that the factor most consistently associated with vaccination refusal was parental perception that the vaccine caused side-effects (Chapter 2). While there is ample evidence that parents choose not to vaccinate their child for fear of side-effects (91, 93, 95, 182), the root cause of parental perception of side-effects from vaccination is unclear. Although some side-effects may occur as a result of the pharmacological action of the vaccine, others may reflect pre-existing or coincidental symptoms that are misattributed to the vaccine, and still others may arise as a result of psychological factors such as parental expectations, or other psychological mechanisms such as information processing biases. Little research into why parents perceive symptoms in their children exists. Where it does, research is heterogeneous and poor quality, making it difficult to state conclusively how factors are associated with parental symptom perception (Chapter 3). In particular, the expectation of side-effects, which may arise from previous experience of side-effects or seeing side-effects in other children, may play a key role in parental perception of side-effects from vaccination. Parental anxiety, general beliefs and attitudes about vaccinations, and biases of information processing may also influence perception of side-effects following vaccination. Diminishing parental perception of side-effects from vaccination, by influencing factors associated with side-effect perception, could be a novel target for interventions aiming to increase vaccine uptake. Furthermore, diminishing parental perception of side-effects from vaccination could positively impact parental medication beliefs and future medication adherence.

While many biases of information processing exist, for my thesis I have chosen to investigate the influence of interpretation bias on vaccination behaviour for the following reasons. First, while parental perception of symptoms is likely impacted more by attention biases than perception of symptoms in oneself, evidence for the role of attention biases in symptom perception was mixed. I

found stronger evidence for a potential causal role of interpretation bias (Chapter 3). Second, bias modification shows more consistent, stronger effects for interpretation than attention (400). Bias modification is the logical next step for research if an association between interpretation bias and vaccination behaviour is identified. Third, knowing how people interpret information related to child vaccination could help inform the phrasing of official vaccine communications.

The content-specific nature of biases suggests that information processing biases will be strongest in those areas most closely related to vaccination behaviour. I have identified two facets of vaccination behaviour which might be particularly important here: the source of the health threat (man-made or naturally-occurring) and the subject of the health threat (self- or child-relevant).

The literature reviews presented in Chapters 2 and 3 resulted in a series of research aims and hypotheses that I investigated using a cross-sectional survey of parents whose child was eligible to receive the influenza vaccine in England during the 2015/16 influenza season (Chapter 5) and a prospective cohort study of parents vaccinating their child for influenza in primary care surgeries in South London during the 2016/17 influenza season, who were followed up in the 2017/18 influenza season (Chapter 6).

4.1 Hypotheses relating to vaccine uptake

I investigated whether psychological factors were associated with uptake of the child influenza vaccine and vaccination intention for the following season. Specifically, I hypothesised that parents a) who refused the vaccine and b) did not intend to vaccinate their child the following year would be more likely to:

1. believe that influenza was benign;
2. have negative beliefs and attitudes about vaccinations in general and the child influenza vaccine in particular;
3. Have different patterns of interpretation biases, specifically:
    a. have more negative interpretation biases for man-made health threats as opposed to naturally-occurring health threats (source of health threat);

b. have similar negative biases for self-relevant and child-relevant health threats (subject of health threat);

4. have no history of child influenza vaccination.

All hypotheses were investigated in the cross-sectional study (Chapter 5).

As exploratory analyses, I also used the cross-sectional study to investigate potential associations between parent and child personal and clinical characteristics and vaccine uptake and vaccination intention.

4.2 Hypotheses relating to re-vaccination

I investigated whether psychological factors were associated with child influenza re-vaccination intention and actual re-vaccination behaviour in the next influenza season among parents who had already vaccinated their child once. Specifically, I hypothesised that parents who did not re-vaccinate their child and who did not intend to re-vaccinate their child the following year would be more likely to:

1. have perceived side-effects from vaccination;
2. have perceived more severe side-effects;
3. be more worried about the side-effects that were perceived;
4. have heard from a healthcare worker in the vaccination appointment that the vaccine caused side-effects;
5. think their child was more sensitive to medicines after they had been vaccinated for influenza;
6. have less trust in healthcare workers after their child had been vaccinated for influenza;
7. have different patterns of interpretation bias, specifically:
    a. have more negative interpretation biases for man-made health threats as opposed to naturally-occurring health threats;
    b. have similar negative biases for self-relevant and child-relevant health threats.

8. In addition, I hypothesised that parents who did not intend to re-vaccinate their child the following year would be less likely to re-vaccinate their child.

All hypotheses were investigated in the prospective cohort study (Chapter 6).

As exploratory analyses, I also used the prospective cohort study to investigate potential associations between parent and child personal and clinical characteristics and actual and intended re-vaccination for influenza in children who had already been vaccinated.

4.3 Hypotheses relating to parental side-effect perception

I investigated whether psychological factors were associated with parental perception of side-effects following one's child's influenza vaccination. Specifically, I hypothesised that parents who reported side-effects from the child influenza vaccine would be more likely to:

1. report symptoms in the child before vaccination;
2. expect their child to develop side-effects from vaccination;
3. have negative beliefs about medicines;
4. think their child was more sensitive to medicines;
5. have increased modern health worries;
6. believe that influenza was benign;
7. have negative beliefs and attitudes about vaccinations in general and the child influenza vaccine in particular;
8. have increased trait anxiety;
9. have increased negative affect;
10. have increased neuroticism;
11. have increased pessimism;
12. have decreased positive affect;
13. have decreased optimism;

14. have different patterns of interpretation bias, specifically:

    a. have more negative interpretation biases for man-made health threats as opposed to naturally-occurring health threats;

    b. have similar negative biases for self-relevant and child-relevant health threats.

15. I also hypothesised that parental expectations might mediate the relationship between psychological predictors and parental perception of side-effects.

Hypothesis six, seven and fourteen were investigated in the cross-sectional study (Chapter 5). All hypotheses were investigated in the prospective cohort study (Chapter 6).

As exploratory analyses, I also used the cross-sectional and prospective cohort studies to investigate potential associations between parent and child personal and clinical characteristics and parental perception of side-effects from vaccination.

Chapter 5. Cross-sectional study

As we have seen, many psychological, social and contextual factors are associated with not vaccinating, with the most consistent reason given for refusing vaccination being the fear of side-effects (Chapter 2). Biases and heuristics have long been implicated in vaccine uptake (101, 102), but the influence of information processing biases has not yet been investigated. In Chapter 4, I hypothesised that more benign beliefs about influenza and more negative beliefs and attitudes about the vaccine; negative interpretation biases; and parent and child personal and clinical characteristics would be associated with child influenza vaccine uptake in 2015/16 and vaccination intention in 2016/17 (Hypothesis 4.1.1, Hypothesis 4.1.3).

While symptoms are commonly reported following vaccinations, their causes are not always straightforward. Although some may be directly attributable to the vaccine, pre-existing or coincidental symptoms may be misattributed to the vaccine, while still others may occur due to a 'nocebo' effect. There is good evidence that psychosocial factors influence subjective symptom perception. However, there is less research investigating the influence of psychosocial factors on parental perception of symptoms in one's child. Where it does exist, research is highly heterogeneous and mostly poor quality (Chapter 3). Information processing biases may also play a role in parental symptom perception (385). However, to the best of my knowledge there is no research investigating whether cognitive biases are associated with parental perception of vaccination side-effects. In Chapter 4, I hypothesised that more benign beliefs about influenza and more negative beliefs and attitudes about the vaccine; negative interpretation biases; and parent and child personal and clinical characteristics would be associated with parental perception of side-effects from the child influenza vaccination in those who were vaccinated in 2015/16 (Hypothesis 4.3.6, Hypothesis 4.3.14). I also hypothesised that those who perceived side-effects from vaccination, in particular those who perceived more severe side-effects and who were more worried about side-effects perceived, would be less likely to intend to re-vaccinate their child in 2016/17.

Research into terms used to describe the incidence of side-effects shows that using verbal descriptors of risk, such as those used in current communications (73, 401), often leads to heightened estimations of incidence (272, 402, 403). Other vaccine-specific terms often used in current communications, such as 'effectiveness' are also likely to be poorly understood. Thus, I used the same study to test whether terms currently used to describe the incidence of side-effects and the effectiveness of the child influenza vaccine were understood by parents.

For this chapter, I conducted a nationally-representative cross-sectional study of parents of children eligible for the influenza vaccine in the 2015/16 influenza season. I investigated whether psychological factors were associated with child influenza vaccine uptake in 2015/16; parental perception of side-effects from vaccination in those who were vaccinated; and vaccination intention for 2016/17.

5.1 Method

5.1.1 Design

I commissioned the market research company Ipsos MORI to conduct an online survey of parents or guardians of children aged between two and seven years on 31st August 2015 living in England. Data collection took place between 16th and 30th March 2016, after the end of England's child influenza vaccination campaign for that year (404).

5.1.2 Participants and recruitment

Ipsos MORI recruited participants from an existing panel of people willing to take part in internet surveys (n=160,000 in England). Invitations to take part were sent to those who had previously indicated that they were a parent or legal guardian of a child born between 1st September 2008 and 31st August 2013 living in England. Quotas based on parent age and gender (combined), region, working status, gender of child and age of child were set to reflect the known demographic profile of parents of children in England (405). Participants spoke fluent English and were aged eighteen or over. Panel participants typically receive points for every survey they complete: for this survey, participants received points worth 75p.

5.1.2.1 *Selection of index child*

Where participants had two or more eligible children, the survey software chose one child for them to think about when answering questions, based on the need to fill quotas for child age. If parents had two children of the same age, they were asked to choose one to think about for the duration of the survey.

5.1.3 Materials

Full study materials can be found in Appendix 5.

5.1.3.1 *Vaccine uptake in 2015/16*

Participants were asked whether their child 'had received the influenza vaccine this winter (2015/16),' answering either 'yes,' 'no' or 'don't know.' Parents were also asked to state their main reasons for vaccinating or not vaccinating their child.

5.1.3.2 *Side-effect perception*

Participants whose child had been vaccinated were asked whether the child had experienced any out of a list of 23 symptoms 'because of the child flu vaccine.' I included symptoms listed as potential vaccine side-effects in the patient information leaflet by the manufacturer (73), common symptoms taken from the Patient Health Questionnaire (PHQ-15) (406), other symptoms suggested by the literature (dizziness) (246), and a more general non-specific symptom (the child being 'not themselves') that was recommended when the materials were piloted with eleven parents. Participants who reported symptoms were asked how severe, overall, the symptoms had been and how worried they had been about them.

5.1.3.3 *Vaccination intention for 2016/17*

Participants were asked whether they agreed or disagreed with the statements 'I **want** [child] to be vaccinated for flu next year' and 'I **intend** [child] to be vaccinated for flu next year.' Answers were given on a five-point Likert scale from 'strongly disagree' to 'strongly agree.' This approach was taken from Payaprom et al. (407).

5.1.3.4 *Beliefs and attitudes about influenza and the child influenza vaccine*

Participants' beliefs and attitudes about influenza and the child influenza vaccine were measured using nineteen items adapted from previous work (408); these statements were rated on a five-point Likert scale from 'strongly agree' to 'strongly disagree.' Statements referred to parents' beliefs about the vaccine, including whether they thought it to be safe; effective; to cause long- or short-term side-effects; possible interactions with other medication taken by the child; and whether it suited religious or cultural beliefs. Statements also referred to possible vaccine recommendations made by health professionals and friends or family and whether the vaccine campaign was 'just about making money for the manufacturers.' Beliefs about influenza were measured by asking whether parents thought influenza would be a serious illness for themselves, the child, or someone else in the child's household as well as the child's perceived vulnerability to influenza. Higher scores to belief and attitude statements indicated a more positive belief or attitude.

5.1.3.5 *Terminology used in vaccine communications*

Understanding of current communications regarding the effectiveness of the vaccine was assessed by one item asking participants to imagine that the child influenza vaccine was '50% effective.' Participants endorsed one of five options for what this means, including the correct answer 'if a child had a 50% chance of catching flu before being vaccinated, they now have half that chance (i.e. 25%).'

I included four items to assess understanding of terms used to communicate the incidence of acute side-effects. The four items described side-effects that were 'very common' (runny or stuffy nose), 'common' (fever), 'uncommon' (rash) and 'very rare' (severe allergic reaction) as indicated by the patient information leaflet for Fluenz Tetra (73). These terms are recommended for use in patient information leaflets by European Commission guidelines and are intended to reflect side-effects that affect more than one in ten patients (very common), up to one in ten (common), up to one in 100 (uncommon) and up to one in 10,000 (very rare) (409). Items stated, for example, that 'the patient information leaflet mentions that fever is a common side-effect' and asked participants to estimate how many out of 10,000 vaccinated children would develop the specified

symptom. The patient information leaflet for Fluenz Tetra does not describe any 'rare' side-effects, so participants' understanding of this term was not assessed.

5.1.3.6 *Interpretation bias*

Interpretation bias can be measured using a wide range of tasks in which participants are asked to interpret ambiguous stimuli. If participants consistently interpret items negatively, they are said to have a negative interpretation bias. Many different variations of interpretation bias tasks exist, in which participants are required to unscramble sentences, or interpret ambiguous words, images or scenarios (see Schoth et al. (410) for a review of tasks). Generally, participants are presented with several ambiguous stimuli which can be interpreted either positively or negatively. While it depends on the individual tasks, negative interpretation bias tends to be calculated as the proportion of ambiguous stimuli interpreted in a negative manner. Positive interpretation biases can also be measured, by calculating the proportion of ambiguous stimuli interpreted positively.

I used the scrambled sentences task (411) to measure interpretation biases in this study due to its sensitivity to individual differences (191, 412) and good reliability (413). Items consisted of six words presented in a fixed-random order which had to be unscrambled to create a meaningful five-word statement. Each word string could be resolved into either a positive or a negative statement. For example, the words 'illness a flu serious is minor' could produce either 'flu is a serious illness' or 'flu is a minor illness.' Participants were given two minutes to complete ten items. Items were presented in a random order.

Given the theoretical differences between domains that might be most associated with child influenza vaccination, I developed materials to test interpretation biases specific to a) the *source* of a health threat (two levels: man-made or naturally-occurring) and b) the *subject* of a health threat (two levels: self-relevant or child-relevant). For the source of the health threat items, man-made health threats (five items) included vaccination, medicines, side-effects, new inventions and mobile phones, while naturally-occurring health threats (five items) included influenza, illness, bacteria, germs and getting a sun-tan. For the subject of a health threat items, self-relevant health threats (five items) included physical

health, feeling tired and suffering aches and pains, and child-relevant health threats (five items) included physical health, development and illness. Items were pilot tested with four parents of children aged two to seven years for validity and were revised as necessary. The final twenty items are provided in Appendix 6.

Participants completed the scrambled sentence task under cognitive load, as this has previously been shown to prevent strategic inhibition of biases and increase the sensitivity of the measure to interpretation bias (411). Before unscrambling the sentences, participants memorized a six-digit number. Participants were instructed not to use memory aides (such as writing the number down). At the end of the task, participants were asked to recall the number. Participants were also asked to report any strategy they used to help them recall the number.

Negative interpretation bias scores were calculated by dividing the number of negative statements produced by the total number of items attempted. Higher bias scores indicated higher negative interpretation bias.

5.1.3.7 *Personal and clinical characteristics*

Participants were asked for their age, gender, employment status, highest level of education, total household income, ethnicity and whether they had a chronic illness. The child's age, gender, and whether they were first-born or had a chronic illness were also recorded.

5.1.4 Piloting materials

Questionnaire materials were piloted with eleven parents of children aged two to seven years for understanding; items were amended according to problems identified. Interpretation bias items were piloted on four parents of children aged two to seven years for validity and revised if parents had difficulty unscrambling them.

5.1.5 Ethical approval

The study was approved by the King's College London Psychiatry, Nursing and Midwifery Research Ethics subcommittee (reference number HR-15/16-2132).

5.1.6 Procedure

Ipsos MORI sent an email to their panel members identified as parents inviting them to complete the study materials online. Panel members taking part were presented with an online information sheet and provided electronic consent through the use of a tick box.

Participants then completed a questionnaire (approximately ten minutes long) which asked about child influenza vaccine uptake, parental perception of side-effects, parental beliefs and attitudes about influenza and the vaccine, and personal and clinical characteristics.

Participants then completed interpretation bias materials (scrambled sentence task, ten items) pertaining to either the source of the health threat or the subject of the threat. Each participant was allocated by the survey software to either the source or subject items based on which version had the fewest number of respondents at that point.

5.1.7 Power

I intended to recruit 1,000 participants to provide me with a sample error of approximately plus or minus 3%.

Only a subset of survey participants completed interpretation bias materials to a satisfactory level and were included in the analyses presented here. I used G*Power (414) to run post-hoc power analyses for each of the interpretation bias analyses. For the vaccine uptake in 2015/16 analyses, I based power analyses on the use of a repeated measures ANOVA. Using a-priori parameters of two groups and two measures, with the correlation between measures being 0.5 and an alpha of .05 I had over 99.9% power to detect a medium effect size (f=0.25) for a within-between interaction in analyses pertaining to the source of the health threat (n=153) and the subject of the health threat (n=159).

For the side-effect perception analyses, I based power analyses on the use of a repeated measures ANOVA. Using a-priori parameters of two groups and two measures, with the correlation between measures being 0.5 and an alpha of .05, I had 99.7% power to detect a medium effect size between groups (f=0.25) for a within-between interaction in analyses pertaining to the source of the health threat

(n=79) and 99.2% power in analyses pertaining to the subject of the health threat (n=159).

For the vaccination intention in 2016/17 analyses, I based power analyses on the use of a fixed effects multiple linear regression. Using a-priori parameters of three tested predictors and five total predictors, with an alpha of .05, I had 98.6% power to detect a medium effect size (f^2=0.15) in analyses pertaining to the source of the health threat (n=153) and 98.9% power in analyses pertaining to the subject of the health threat (n=159).

5.1.8 Analysis

Where relevant, I excluded data from participants who did not know or could not remember if their child had been vaccinated or had experienced side-effects. Scores for the two items assessing intention to vaccinate in 2016/17 were combined to produce an intention score from two to ten (407), with a higher score indicating a stronger intention. If participants had answered 'don't know' to one or both intention questions they were excluded from the intention analyses. I defined a score of six or lower as indicating a low intention to vaccinate again in 2016/17, and a score of seven or more as high intention.

I recoded beliefs and attitudes about influenza and the vaccine as 'agree' or 'disagree'. Responses of 'don't know' and 'neither agree nor disagree' were treated as missing data.

Because rates of reported vaccine uptake, perceived side-effects, and intention to vaccinate the child did not change by more than 1% when using data weighted by age, gender, region and working status, I used unweighted data for my analyses.

I used binary logistic regressions to identify whether influenza vaccine uptake in 2015/16 and side-effect perception were associated with: beliefs and attitudes about influenza and the child influenza vaccine; and personal and clinical characteristics. Multivariate logistic regressions were used to calculate the same associations adjusting for personal characteristics. I used linear regressions to identify whether vaccination intention was associated with: beliefs and attitudes about influenza and the child influenza vaccine; perception of side-effects from vaccination in 2015/16, perceived severity of side-effects and worry about side-

effects; and personal and clinical characteristics. A second set of linear regressions adjusted for personal characteristics. Only results of multivariate analyses are reported narratively; results of univariate analyses are shown in the tables. Where analyses relied on under ten participants in one cell, these are not reported narratively unless they have a material impact on results.

5.1.8.1 *Interpretation bias*

Participants were excluded from the analyses if they did not complete interpretation bias task materials adequately, defined as 40% missing data from any domain (man-made or naturally-occurring health threats; self-relevant or child-relevant health threats), or if participants reported using a strategy to remember the number. Data for interpretation bias tasks pertaining to the source and the subject of the health threat were analysed separately.

To investigate whether there was an association between child influenza vaccine uptake and interpretation bias, I ran two mixed-model, repeated measures ANOVAs on bias scores with vaccination status as a between-participant factor (uptake, or no uptake). In one ANOVA, the within participant factor was the source of the health threat (two levels: man-made and naturally-occurring), whereas in the other it was the subject of the health threat (two levels: self-relevant and child-relevant).

To investigate whether there was an association between parental perception of side-effects from vaccination and interpretation bias, I ran two mixed-model, repeated measures ANOVAs with side-effect perception as a between-participant factor (side-effects perceived, or no side-effects perceived). In one ANOVA, the within participant factor was the source of the health threat (two levels: man-made and naturally-occurring), whereas in the other it was the subject of the health threat (two levels: self-relevant and child-relevant).

To investigate the association between vaccination intention and interpretation bias, I ran two hierarchical linear regressions with bias score as the dependent variable. Vaccination intention, health threat (source of health threat: man-made and naturally-occurring; subject of health threat: self-relevant and child-relevant) and an intention*health threat interaction term were entered as the independent variables.

For all interpretation bias analyses, personal and clinical characteristics (parent gender, parent age, parent employment, total household income, parent education, parent ethnicity, parent chronic illness, child gender, first-born child, child age and child chronic illness) were investigated to see whether there was a univariate association ($p \leq .05$) with outcome variables. Where personal and clinical characteristics were associated with outcome variables, they were entered into the analyses as covariates. In regression analyses, covariates were entered into the regression model as the first block; predictor variables were entered into the model as the second block. Controlling for all personal and clinical characteristics was considered too conservative in interpretation bias analyses due to the smaller sample sizes and innovative nature of the research (e.g. (415)).

5.1.9 Statistical software

I analysed data using SPSS 22 (416).

5.2 **Results**

5.2.1 Participants

Of 11,563 people emailed the link to the survey, 1,310 began it. After removing those who did not complete the survey (n=268), who completed suspiciously quickly or who provided identical answers to multiple consecutive questions ('speeding' or 'straightlining;' n=34), or who experienced a technical malfunction during the survey (n=7), 1001 parents or guardians completed the study (response rate = 8.7%).

Personal characteristics of participants and their children are shown in Table 6.

Table 6. Parent and child personal and clinical characteristics and associations with influenza vaccine uptake in 2015/16 and vaccination intention for 2016/17

Participant characteristics	Level	Influenza vaccine uptake in 2015/16				Vaccination intention for 2016/17		
		Vaccinated n=529, n (%)	Not vaccinated n=438, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Total=950. N, M, SD	B (95% CI)	Adjusted B (95% CI)[a]
Parent gender	Female	317 (55.9)	247 (44.1)	1.16 (0.89 to 1.50)	1.13 (0.79 to 1.64)	N=548, M=7.66, SD=2.59	0.06 (-0.26 to 0.38)	-0.06 (-0.39 to 0.27)
	Male	212 (52.6)	191 (47.4)	Reference	Reference	N=402, M=7.59, SD=2.35	Reference	Reference
Parent age	45+	53 (42.1)	73 (57.9)	0.47 (0.31 to 0.71)*	0.84 (0.47 to 1.50)	N=119, M=7.10, SD=2.59	-0.74 (-1.25 to -0.23)*	-0.35 (-0.88 to 0.17)
	35-44	238 (53.0)	211(47.0)	0.73 (0.56 to 0.96)*	0.88 (0.60 to 1.28)	N=440, M=7.58, SD=2.48	-0.26 (0-.60 to 0.08)	-0.05 (-0.38 to 0.29)
	18-34	238 (60.7)	154 (39.3)	Reference	Reference	N=391, M=7.84, SD=2.45	Reference	Reference
Parent employment	Working	403 (55.0)	330 (45.0)	1.05 (0.78 to 1.41)	0.98 (0.63 to 1.52)	N=726, M=7.62, SD=2.40	-0.04 (-0.41 to 0.34)	-0.15 (-0.55 to 0.25)
	Not working	126 (53.8)	108 (46.2)	Reference	Reference	N=224, M=7.66, SD=2.78	Reference	Reference
Total household income before tax and other deductions	≥£30,000	311 (54.3)	262 (46.7)	0.91 (0.69 to 1.19)	0.88 (0.60 to 1.29)	N=565, M=7.63, SD=2.39	-0.10 (-0.44 to 0.23)	-0.07 (-0.41 to 0.28)
	Under <£30,000	191 (56.7)	146 (43.3)	Reference	Reference	N=331, M=7.74, SD=2.60	Reference	Reference
Parent highest educational or professional qualification	Degree or higher (Bachelors, Masters, PhD)	289 (55.5)	232 (44.5)	1.06 (0.82 to 1.37)	1.18 (0.82 to 1.71)	N=513, M=7.66, SD=2.35	0.03 (-0.29 to 0.35)	0.02 (-0.31 to 0.35
	GCSE/vocational/A-level/No formal qualifications	230 (54.1)	195 (45.9)	Reference	Reference	N=415, M=7.62, SD=2.63	Reference	Reference
Parent ethnicity	Black and Minority	66 (48.9)	69 (51.1)	0.75 (0.52 to 1.08)	0.69 (0.42 to 1.12)	N=133, M=7.49, SD=2.50	-0.20 (-0.65 to 0.26)	-0.16 (-0.61 to 0.28)
	White	456 (56.0)	358 (44.0)	Reference	Reference	N=798, M=7.68, SD=2.48	Reference	Reference
Parent chronic illness	Present	183 (59.6)	124 (40.4)	1.34 (1.02 to 1.77)*	1.06 (0.71 to 1.57)	N=308, M=7.84, SD=2.34	0.32 (-0.19 to 0.66)	0.12 (-0.23 to 0.47)
	None	343 (52.4)	312 (47.6)	Reference	Reference	N=639, M=7.52, SD=2.56	Reference	Reference

Child gender	Female	270 (55.0)	221 (45.0)	1.02 (0.80 to 1.32)	1.23 (0.87 to 1.73)	N=484, M=7.63, SD=2.53	0.01 (-0.31 to 0.33)	0.15 (-0.16 to 0.46)
	Male	259 (54.4)	217 (45.6)	Reference	Reference	N=466, M=7.62, SD=2.46	Reference	Reference
First-born child	Yes	319 (61.2)	202 (38.8)	1.78 (1.37 to 2.29)*	1.35 (0.95 to 1.93)	N=517, M=7.78, SD=2.35	0.34 (0.02 to 0.66)*	-0.05 (-0.37 to 0.27)
	No	210 (47.1)	236 (53.9)	Reference	Reference	N=433, M=7.45, SD=2.64	Reference	Reference
Child age	Range 2 to 7 years	N=529, M=4.41, SD=1.71	N=438, M=4.66, SD=1.66	0.92 (0.85 to 0.99)*	0.96 (0.87 to 1.06)	N=950, M=7.63, SD=2.49	-0.09 (-0.18 to 0.01)	-0.04 (-0.13 to 0.05)
Child chronic illness	Present	103 (66.9)	51 (33.1)	1.84 (1.28 to 2.64)*	1.36 (0.82 to 2.26)	N=158, M=8.04, SD=2.15	0.51 (0.08 to 0.93)*	0.02 (-0.42 to 0.46)
	None	421 (52.4)	383 (47.6)	Reference	Reference	N=784, M=7.54, SD=2.55	Reference	Reference
Child previous influenza vaccine	Yes	434 (81.0)	102 (19.0)	17.13 (12.35 to 23.76)*	15.54 (11.00 to 21.96)*	N=537, M=8.61, SD=1.72	2.37 (2.08 to 2.67)*	2.25 (1.94 to 2.57)*
	No	79 (19.9)	318 (80.1)	Reference	Reference	N=369, M=6.24, SD=2.78	Reference	Reference

*$p \leq .05$

[a] Adjusting for all other personal characteristics (both parent and child)

5.2.2 Vaccine uptake in 2015/16

529 participants (52.8%) reported that their child had been vaccinated for influenza in the 2015/16 influenza season, 438 (43.8%) reported that their child had not been vaccinated and 34 (3.4%) did not know. Participants' reasons for vaccinating or not vaccinating their child are reported in Appendix 7. The most common reason for vaccinating was to protect the child from influenza, cited by 61.2% of participants who vaccinated their child. The most commonly reported reason for not vaccinating was because participants thought that the child was generally healthy and they were not overly worried about them catching influenza (43.2%), followed by the perception that the vaccine causes side-effects (21.7%).

Associations between personal and clinical characteristics, beliefs and attitudes about influenza and the vaccine and vaccination uptake in the 2015/16 season are reported in Table 6 and Table 7. When controlling for personal and clinical characteristics, participants whose child had a previous influenza vaccination; who believed the influenza vaccine to be effective; who perceived the child to be susceptible to influenza; who had a health professional recommend that the child should be vaccinated; and who perceived influenza to be a serious illness for the child had increased odds of vaccine uptake. Factors associated with lower likelihood of uptake included: participants feeling that they did not know enough about the vaccine; perceiving the vaccine to be unsafe; believing the vaccination campaign to be only about making money for the manufacturers; believing that the vaccine caused short-term side-effects and long-term health problems; believing that yearly vaccination would overload the child's immune system; not liking vaccines in general; and believing yearly influenza vaccinations to be too much of an ongoing time commitment.

Table 7. Parental beliefs and attitudes about influenza and the child vaccine and associations between vaccine uptake in 2015/16 and vaccination intention for 2016/17

Statement	Level	Influenza vaccine uptake in 2015/16				Vaccination intention for 2016/17		
		Vaccinated n=529, n (%)	Not vaccinated n=438, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Total=950. N, M, SD	B (95% CI)	Adjusted B (95% CI)[a]
The child flu vaccine has not been tested enough for me to feel it is safe	Agree	89 (34.9)	166 (65.1)	0.15 (0.11 to 0.22)*	0.16 (0.10 to 0.26)*	N=251, M=6.48, SD=2.80	-2.34 (-2.68 to -2.00)*	-1.78 (-2.12 to -1.44)*
	Disagree	315 (77.8)	90 (22.2)	Reference	Reference	N=410, M=8.82, SD=1.64	Reference	Reference
The child flu vaccine can cause unpleasant short-term side-effects	Agree	206 (47.5)	228 (52.5)	0.23 (0.16 to 0.35)*	0.26 (0.16 to 0.43)*	N=423, M=7.13, SD=2.73	-1.76 (-2.18 to -1.35)*	-1.37 (-1.77 to -0.96)*
	Disagree	151 (79.5)	39 (20.5)	Reference	Reference	N=192, M=8.89, SD=1.55	Reference	Reference
The child flu vaccine can cause long-term health problems	Agree	86 (45.5)	103 (54.5)	0.31 (0.22 to 0.45)*	0.26 (0.15 to 0.42)*	N=188, M=6.64, SD=2.92	-2.05 (-2.43 to -1.67)*	-1.83 (-2.22 to -1.45)*
	Disagree	293 (72.9)	109 (27.1)	Reference	Reference	N=402, M=8.69, SD=1.72	Reference	Reference
The flu vaccine would interact with other medications that [child] is currently taking	Agree	71 (64.5)	39 (35.5)	1.49 (0.98 to 2.26)	0.74 (0.41 to 1.32)	N=109, M=8.21, SD=1.96	0.55 (0.04 to 1.06)*	0.05 (-0.46 to 0.55)
	Disagree	370 (55.1)	302 (44.9)	Reference	Reference	N=653, M=7.66, SD=2.59	Reference	Reference
Vaccinating [child] against flu each year will overload his/her immune system	Agree	90 (45.0)	110 (55.0)	0.37 (0.27 to 0.52)*	0.27 (0.16 to 0.44)*	N=193, M=6.92, SD=2.67	-1.62 (-2.00 to -1.25)*	-1.43 (-1.80 to -1.05)*
	Disagree	316 (68.7)	144 (31.3)	Reference	Reference	N=464, M=8.54, SD=2.03	Reference	Reference
Another child I know had side-effects from the vaccine	Agree	113 (58.9)	79 (41.1)	1.10 (0.79 to 1.54)	0.647 (0.41 to 1.02)	N=193, M=7.49, SD=2.58	-0.48 (-0.88 to -0.73)*	-0.83 (-1.21 to -0.44)*
	Disagree	312 (56.5)	240 (43.5)	Reference	Reference	N=536, M=7.96, SD=2.41	Reference	Reference
A health professional has recommended that [child] should be vaccinated	Agree	284 (76.3)	88 (23.7)	6.08 (4.37 to 8.47)*	3.61 (2.36 to 5.50)*	N=375, M=8.61, SD=1.98	1.95 (1.59 to 2.30)*	1.11 (0.72 to 1.49)*
	Disagree	112 (33.6)	211 (66.4)	Reference	Reference	N=300, M=6.66, SD=2.75	Reference	Reference
A health professional has recommended that [child] shouldn't be vaccinated	Agree	84 (62.7)	50 (37.3)	1.24 (0.84 to 1.81)	0.853 (0.51 to 1.44)	N=131, M=7.95, SD=2.28	0.16 (-0.30 to 0.63)	-0.13 (0.58 to 0.32)
	Disagree	381 (57.6)	280 (42.4)	Reference	Reference	N=648, M=7.79, SD=2.50	Reference	Reference

A friend/relative has recommended that [child] shouldn't be vaccinated	Agree	90 (60.0)	60 (40.0)	1.14 (0.79 to 1.64)	0.73 (0.45 to 1.18)	N=146, M=7.77, SD=2.33	-0.07 (-0.51 to 0.38)	-0.41 (-0.85 to 0.02)
	Disagree	363 (56.8)	276 (43.2)	Reference	Reference	N=627, M=7.84, SD=2.51	Reference	Reference
If I don't vaccinate [child], then [child] will get flu	Agree	225 (74.8)	76 (25.2)	8.79 (6.00 to 12.87)*	4.46 (2.66 to 7.48)*	N=310, M=8.85, SD=1.62	3.42 (3.06 to 3.78)*	2.90 (2.48 to 3.31)*
	Disagree	66 (25.2)	196 (74.8)	Reference	Reference	N=249, M=5.43, SD=2.67	Reference	Reference
Flu would be a serious illness for [child]	Agree	370 (62.2)	225 (37.8)	2.60 (1.84 to 3.67)*	1.66 (1.03 to 2.66)*	N=583, M=8.26, SD=2.09	2.01 (1.61 to 2.41)*	1.40 (0.99 to 1.81)*
	Disagree	69 (38.8)	109 (61.2)	Reference	Reference	N=170, M=6.25, SD=3.04	Reference	Reference
Flu would be a serious illness for me	Agree	287 (62.0)	176 (38.0)	2.14 (1.57 to 2.91)*	1.40 (0.92 to 2.13)	N=255, M=8.26, SD=2.07	1.61 (1.24 to 1.98)*	0.97 (0.60 to 1.35)*
	Disagree	113 (43.3)	148 (56.7)	Reference	Reference	N=452, M=6.65, SD=2.93	Reference	Reference
Flu would be a serious illness for someone living in [child]'s household	Agree	301 (61.6)	188 (38.4)	1.94 (1.41 to 2.69)*	1.36 (0.87 to 2.12)	N=480, M=8.24, SD=2.19	1.78 (1.38 to 2.17)*	1.27 (0.88 to 1.66)*
	Disagree	98 (45.2)	119 (54.8)	Reference	Reference	N=207, M=6.47, SD=2.96	Reference	Reference
Having the child flu vaccine is an effective way of preventing [child] from catching flu	Agree	427 (71.6)	169 (28.4)	8.28 (5.27 to 13.01)*	4.56 (2.58 to 8.08)*	N=599, M=8.75, SD=1.63	4.14 (3.77 to 4.51)*	3.43 (3.03 to 3.82)*
	Disagree	29 (23.4)	95 (76.6)	Reference	Reference	N=118, M=4.62, SD=2.77	Reference	Reference
I don't like [child] having vaccinations in general	Agree	103 (47.2)	115 (52.8)	0.53 (0.38 to 0.73)*	0.53 (0.34 to 0.82)*	N=209, M=6.71, SD=2.95	-1.55 (-1.96 to -1.15)*	-1.34 (-1.73 to -0.95)*
	Disagree	308 (63.0)	181 (37.0)	Reference	Reference	N=482, M=8.26, SD=2.23	Reference	Reference
I don't know enough about the child flu vaccine	Agree	124 (32.8)	254 (67.2)	0.14 (0.10 to 0.20)*	0.16 (0.10 to 0.25)*	N=362, M=6.80, SD=2.61	-1.69 (-2.06 to -1.32)*	-1.08 (-1.45 to -0.70)*
	Disagree	242 (77.3)	71 (22.7)	Reference	Reference	N=319, M=8.49, SD=2.23	Reference	Reference
Vaccinating [child] against flu each year is too much of an ongoing time commitment	Agree	82 (60.3)	54 (39.7)	1.00 (0.68 to 1.46)	0.59 (0.35 to 1.00)*	N=137, M=7.74, SD=2.26	-0.22 (-0.67 to 0.23)	-0.48 (-0.94 to -0.03)*
	Disagree	381 (60.3)	251 (39.7)	Reference	Reference	N=619, M=7.96, SD=2.47	Reference	Reference
The child flu vaccine does not suit my religious or cultural beliefs/values	Agree	74 (62.2)	45 (37.8)	1.24 (0.83 to 1.86)	0.93 (0.54 to 1.61)	N=118, M=7.57, SD=2.60	-.33 (-0.81 to 0.14)	-0.55 (-1.02 to -0.09)*
	Disagree	385 (57.0)	291 (43.0)	Reference	Reference	N=660, M=7.90, SD=2.38	Reference	Reference
The vaccination campaign is just about making money for the manufacturers	Agree	77 (39.9)	116 (60.1)	0.28 (0.20 to 0.40)*	0.23 (0.14 to 0.38)*	N=192, M=6.20, SD=3.04	-2.39 (-2.77 to -2.00)*	-2.14 (-2.53 to -1.75)*
	Disagree	314 (70.4)	132 (29.4)	Reference	Reference	N=442, M=8.59, SD=1.86	Reference	Reference
Perception of side-effects	Yes					N=212, M=8.62, SD=1.61	-0.54 (-0.78 to -0.31)*	-0.53 (-0.79 to -0.26)*

	No	-	-	-	-	N=301, M=9.17 (1.13)	Reference	Reference
Severity of side-effects	Severe					N=5, M=7.20, SD=1.92	-2.09 (-3.49 to -0.69)*	-2.02 (-3.46 (-0.58)*
	Moderate					N=38, M=7.82, SD=1.98	-1.47 (-2.11 to -0.83)*	-1.59 (-2.27 to -0.91)*
	Mild					N=116, M=8.68, SD=1.28	-0.61 (-1.11 to -0.11)*	-0.63 (-1.18 to -0.08)*
	Very mild	-	-	-	-	N=52, M=9.29, SD=1.60	Reference	Reference
Worry about side-effects	Very worried					N=20, M=8.25, SD=2.63	-0.88 (-1.72 to -0.04)*	-0.72 (-1.60 to 0.16)
	Fairly worried					N=68, M=8.49, SD=1.25	-0.65 (-1.25 to -0.04)*	-0.53 (-1.19 to 0.13)
	Not very worried					N=79, M=8.53, SD=1.56	-0.60 (-1.18 to -0.02)*	-0.44 (-1.07 to 0.19)
	Not at all worried	-	-	-	-	N=46, M=9.13, SD=1.54	Reference	Reference

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child)

5.2.3 Side-effect perception

Of participants who reported that their child had been vaccinated, 215 (41.0%) indicated that their child had experienced at least one side-effect. The most common side-effect reported was runny or stuffy nose (n=84, 16.0%). 'Flu' was reported as a side-effect by 33 participants (6.3%; see Appendix 8 for full results).

Side-effects were described as 'very mild' by 52 participants (24.3%), 'mild' by 118 (55.1%), 'moderate' by 39 (18.2%) and 'severe' by five (2.3%). No-one reported 'very severe' side-effects. Forty-seven (21.8%) participants indicated that they were 'not at all worried' about their child's side-effects, 80 (37.0%) stated that they were 'not very worried,' 68 (31.5%) were 'fairly worried' and 21 (9.7%) were 'very worried.'

Associations between personal and clinical characteristics, beliefs and attitudes about influenza and the vaccine, and perception of side-effects are reported in Table 8 and Table 9. When controlling for all other personal and clinical characteristics, participants were more likely to report side-effects if the child had a chronic illness or was first-born. Participants had increased odds of perceiving side-effects if they: knew another child who had experienced side-effects from the influenza vaccine; thought that the influenza vaccine would interact with other medications that the child was taking; believed that yearly influenza vaccination was too much of an ongoing time commitment; believed that yearly vaccination would overload the immune system; believed the influenza vaccine could cause short-term side-effects or long-term health problems; believed the vaccine went against one's religious or cultural beliefs; believed that the vaccination campaign was just about making money for the manufacturers; had a health professional, friend or relative recommend that the child should not be vaccinated; believed the vaccine to be unsafe; did not like vaccines for the child in general; believed influenza to be a serious illness for the child, oneself or someone in the child's household; or felt they did not know enough about the vaccine. Female participants and older participants were less likely to report side-effects.

Table 8. Parent and child personal and clinical characteristics and associations with perception of side-effects from vaccination

Parent characteristics	**Level**	**Side-effects perceived[1]**			
		Perceived side-effects n=215, n (%)	**No perceived side-effects n=310, n (%)**	**Odds ratio (95% CI)**	**Adjusted odds ratio (95% CI)[a]**
Parent gender	Female	118 (37.6)	196 (62.4)	0.71 (0.50 to 1.01)	0.65 (0.42 to 0.99)*
	Male	97 (46.0)	114 (54.0)	Reference	Reference
Parent age	45+	14 (26.9)	38 (73.1)	0.38 (0.20 to 0.73)*	0.45 (0.21 to 0.96)*
	35-44	84 (35.6)	152 (64.4)	0.57 (0.29 to 0.82)*	0.58 (0.38 to 0.88)*
	18-34	117 (47.6)	129 (52.4)	Reference	Reference
Parent employment	Working	171 (42.8)	229 (57.3)	1.38 (0.91 to 2.09)	0.96 (0.57 to 1.60)
	Not working	44 (35.2)	81 (64.8)	Reference	Reference
Total household income before tax and other deductions	≥£30,000	132 (42.9)	176 (57.1)	1.15 (0.80 to 1.66)	0.93 (0.60 to 1.45)
	Under <£30,000	75 (39.5)	115 (60.5)	Reference	Reference
Parent highest educational or professional qualification	Degree or higher (Bachelors, Masters, PhD)	137 (47.7)	150 (52.3)	1.86 (1.30 to 2.67)*	1.51 (0.97 to 2.36)
	GCSE/vocational/A-level/No formal qualifications	75 (32.9)	153 (67.1)	Reference	Reference
Parent ethnicity	Black and Minority	35 (54.7)	29 (45.3)	1.87 (1.11 to 3.17)	1.55 (0.85 to 2.80)
	White	178 (39.2)	276 (60.8)	Reference	Reference
Parent chronic illness	Present	75 (41.7)	105 (58.3)	1.04 (0.72 to 1.51)	1.05 (0.68 to 1.63)
	None	139 (40.6)	203 (59.4)	Reference	Reference
Child gender	Female	97 (36.3)	170 (63.7)	0.68 (0.48 to 0.96)*	0.74 (0.50 to 1.09)
	Male	118 (45.7)	140 (54.3)	Reference	Reference
First-born child	Yes	151 (47.5)	167 (52.5)	2.02 (1.40 to 2.92)*	1.61 (1.06 to 2.43)*
	No	64 (30.9)	143 (69.1)	Reference	Reference
Child age	Range 2 to 7 years	N=215, M=4.32, SD=1.77	N=310, M=4.46, SD=1.67	0.95 (0.86 to 1.05)	0.95 (0.84 to 1.06)
Child chronic illness	Present	54 (52.4)	49 (47.6)	1.79 (1.16 to 2.76)*	1.67 (1.01 to 2.78)*
	None	159 (38.1)	258 (61.9)	Reference	Reference

[1] When asked why they had not vaccinated their child, three people indicated that they had answered the vaccination question incorrectly and that they had indeed vaccinated their child; these participants' results were recoded, but because of the scripting of the questionnaire, they were not asked side-effect perception questions. One participant stated that their child had been vaccinated could not remember whether they had experienced any side-effects, therefore side-effect perception data for this participant were removed from the analysis As such, side-effect perception data for 525 parents are presented.

Child previous influenza vaccine	Yes	189 (43.8)	243 (56.3)	1.65 (0.99 to 2.75)	1.43 (0.80 to 2.53)
	No	25 (32.1)	53 (67.9)	Reference	Reference

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child)

Table 9. Parental beliefs and attitudes about influenza and the child vaccine and associations with perception of side-effects from vaccination

Statement	Level	Side-effects perceived			
		Perceived side-effects n=215, n (%)	No perceived side-effects n=310, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]
The child flu vaccine has not been tested enough for me to feel it is safe	Agree	59 (66.3)	30 (33.7)	3.99 (2.42 to 6.57)*	3.31 (1.87 to 5.88)*
	Disagree	103 (33.0)	209 (67.0)	Reference	Reference
The child flu vaccine can cause unpleasant short-term side-effects	Agree	131 (63.9)	74 (36.1)	5.45 (3.42 to 8.71)*	6.11 (3.61 to 10.35)*
	Disagree	37 (24.5)	114 (75.5)	Reference	Reference
The child flu vaccine can cause long-term health problems	Agree	63 (73.3)	23 (26.7)	6.32 (3.69 to 10.83)*	5.16 (2.70 to 9.85)*
	Disagree	88 (30.2)	203 (69.8)	Reference	Reference
The flu vaccine would interact with other medications that [child] is currently taking	Agree	56 (78.9)	15 (21.1)	8.05 (4.37 to 14.82)*	7.18 (3.42 to 15.04)*
	Disagree	116 (31.7)	250 (68.3)	Reference	Reference
Vaccinating [child] against flu each year will overload his/her immune system	Agree	68 (75.6)	22 (24.4)	6.68 (3.91 to 11.43)*	5.65 (2.96 to 10.80)*
	Disagree	99 (31.6)	214 (68.4)	Reference	Reference
Another child I know had side-effects from the vaccine	Agree	83 (74.1)	29 (25.9)	8.33 (5.08 to 13.66)*	7.27 (4.11 to 12.83)*
	Disagree	79 (25.6)	230 (74.4)	Reference	Reference
A health professional has recommended that [child] <u>should</u> be vaccinated	Agree	136 (48.4)	145 (51.6)	1.95 (1.23 to 3.10)*	1.66 (0.98 to 2.82)
	Disagree	36 (32.4)	75 (67.6)	Reference	Reference
A health professional has recommended that [child] <u>shouldn't</u> be vaccinated	Agree	61 (73.5)	22 (26.5)	5.29 (3.11 to 9.00)*	4.17 (2.25 to 7.72)*
	Disagree	130 (34.4)	248 (65.6)	Reference	Reference
A friend/relative has recommended that [child] shouldn't be vaccinated	Agree	59 (65.6)	31 (34.4)	3.89 (2.39 to 6.33)*	3.46 (1.94 to 6.15)*
	Disagree	118 (32.9)	241 (67.1)	Reference	Reference
If I don't vaccinate [child], then [child] will get flu	Agree	112 (50.2)	111 (49.8)	1.42 (0.81 to 2.48)	1.11 (0.57 to 2.18)
	Disagree	27 (41.5)	38 (58.5)	Reference	Reference
Flu would be a serious illness for [child]	Agree	164 (44.6)	204 (55.4)	3.40 (1.80 to 6.44)*	2.43 (1.19 to 4.98)*
	Disagree	13 (19.1)	55 (80.9)	Reference	Reference

Flu would be a serious illness for me	Agree	139 (48.4)	148 (51.6)	2.42 (1.51 to 3.90)*	2.45 (1.41 to 4.24)*
	Disagree	31 (27.9)	80 (72.1)	Reference	Reference
Flu would be a serious illness for someone living in [child]'s household	Agree	131 (43.8)	168 (56.2)	1.92 (1.17 to 3.15)*	1.84 (1.04 to 3.25)*
	Disagree	28 (28.9)	69 (71.1)	Reference	Reference
Having the child flu vaccine is an effective way of preventing [child] from catching flu	Agree	169 (39.8)	256 (60.2)	0.572 (0.27 to 1.23)	0.54 (0.22 to 1.28)
	Disagree	15 (53.6)	13 (46.4)	Reference	Reference
I don't like [child] having vaccinations in general	Agree	65 (63.1)	38 (36.9)	3.60 (2.25 to 5.74)*	2.91 (1.71 to 4.94)*
	Disagree	98 (32.2)	206 (67.8)	Reference	Reference
I don't know enough about the child flu vaccine	Agree	64 (52.0)	59 (48.0)	2.09 (1.34 to 3.26)*	2.09 (1.26 to 3.46)*
	Disagree	82 (34.2)	158 (65.8)	Reference	Reference
Vaccinating [child] against flu each year is too much of an ongoing time commitment	Agree	63 (76.8)	19 (23.2)	7.37 (4.22 to 12.87)*	6.16 (3.17 to 11.98)*
	Disagree	117 (31.0)	260 (69.0)	Reference	Reference
The child flu vaccine does not suit my religious or cultural beliefs/values	Agree	56 (75.7)	18 (24.3)	6.45 (3.64 to 11.43)*	4.94 (2.55 to 9.57)*
	Disagree	124 (32.5)	257 (67.5)	Reference	Reference
The vaccination campaign is just about making money for the manufacturers	Agree	56 (72.7)	21 (27.3)	5.23 (3.01 to 9.10)*	4.49 (2.33 to 8.66)*
	Disagree	105 (33.8)	206 (66.2)	Reference	Reference

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child)

5.2.4 Vaccination intention for 2016/17

Six-hundred and sixty-eight (70.3%) participants had a high intention to vaccinate their child in the 2016/17 influenza season. Associations between personal characteristics, beliefs and attitudes about influenza and the child vaccine, and intention to vaccinate in the 2016/17 season are reported in Table 6 and Table 7. The pattern of results for vaccination intention was broadly similar to that for reported uptake. Participants who perceived side-effects following vaccination in the 2015/16 influenza season were less likely to intend to vaccinate their child the following year, as were those who knew another child who had experienced side-effects from the vaccine. In those participants who stated that their child had

experienced a side-effect as a result of the influenza vaccine, perceived severity of the side-effect was associated with decreased intention to vaccinate one's child.

5.2.5 Terminology used in vaccine communications

The correct interpretation of '50% vaccine effectiveness' was selected by 195 participants (19.5%; see Table 10). The most commonly endorsed option was that '50% of children who have the vaccine will be immune to flu' (28.8%, n=288).

Table 10. Table of participants' understanding of the phrase '50% vaccine effectiveness'

Statement	Number of parents (%)
50% of children who have the vaccine will be immune to flu	288 (28.8)
A vaccinated child will have a 50% chance of catching flu	265 (26.5)
If a child had a 50% chance of catching flu before being vaccinated, they now have half that chance (i.e. 25%) [Correct option]	195 (19.5)
Can't tell the difference between the options above	102 (10.2)
Don't know	151 (15.1)

Estimates of the incidence of acute side-effects with different verbal descriptors of risk are reported in Table 11. The median estimate for a 'very common' side-effect was 5,000 in every 10,000 children (1 in 2), 2,000 for 'common side-effects' (1 in 5), 199 for 'uncommon' side-effects (1 in 50) and 50 for 'very rare' side-effects (1 in 200). Interquartile ranges for these estimates overlapped greatly.

Table 11. Table of predicted incidence of side-effects by verbal descriptor of risk out of 10,000 vaccinated children (n = 1001)

	Very common, n (%)	Common, n (%)	Uncommon, n (%)	Very rare, n (%)
0-100	493 (49.3)	219 (21.9)	157 (15.7)	735 (73.4)
101-500	174 (17.4)	76 (7.6)	58 (5.8)	101 (10.1)
501-1000	173 (17.3)	15.7 (15.7)	141 (14.1)	77 (7.7)
1001-2500	68 (6.8)	76 (7.6)	57 (5.7)	28 (2.8)
2501-5000	67 (6.7)	233 (2.3)	203 (20.3)	40 (4.0)
5001-7500	10 (1.0)	100 (10.0)	112 (11.2)	11 (1.1)
7501-10000	16 (1.6)	140 (14.0)	273 (27.3)	9 (0.9)
Median	5000	2000	199	50
Mean (SD)	4406.60 (3523.489)	3325.12 (3150.328)	890.88 (1654.080)	523.22 (1392.375)

5.2.6 Interpretation bias

5.2.6.1 *Participants*

Of the 1001 participants who completed the survey, 500 completed interpretation bias items pertaining to the source of the health threat and 501 completed interpretation bias items pertaining to the subject of the health threat. Many participants did not complete interpretation bias items to levels required for inclusion in the analyses, thus analyses presented are for those who completed the interpretation bias task to an adequate standard (source of health threat, n=158; subject of health threat, n=163). Participant characteristics are shown in Table 12.

Child age differed between those who were assigned to complete items pertaining to the source and subject of the health threat ($t(999)=0.25$, $p=.02$), with those who completed items pertaining to the source of the health threat having older children (M=4.62, SD=1.63) than those who completed items pertaining to the subject of the health threat (M=4.39, SD=1.73; see Appendix 9 for full results). There were no other differences in parent or child personal or clinical characteristics (parent gender, parent age, region, working status, household income, parent education, parent ethnicity, parent chronic illness, first-born child, child age and child chronic illness) between those who were assigned to complete items pertaining to the source and subject of the health threat.

In those who completed bias items pertaining to the source of the health threat, household income differed between those who were and were not included in analyses, with those with a household income of £30,000 or over being more likely to be included in the analyses ($\chi^2(1, n=476)=3.96$, $p=.05$). Ethnicity also varied, with white participants being more likely to be included in analyses than black and minority ethnic groups ($\chi^2(1, n=491)=11.04$, $p=.001$). No other parent or child personal or clinical characteristics differed between those who were and were not included in the analyses for bias pertaining to the source of the health threat.

In those who completed bias items pertaining to the subject of the health threat, ethnicity differed between those who were and were not included in analyses, with white participants being more likely to be included in analyses than black and minority ethnic groups ($\chi^2(1, n=490)=4.75$, $p=.03$). No other parent or child personal or clinical characteristics differed between those who were and were not included in the analyses for bias pertaining to the subject of the health threat.

Table 12. Parent and child personal and clinical characteristics for those included in interpretation bias analyses and associations with vaccine uptake in 2015/16 and perception of side-effects from vaccination

Participant characteristics		**Influenza vaccine uptake in 2015/16**						**Side-effects perceived**					
		Source of health threat (n = 153)			**Subject of health threat (n = 159)**			**Source of health threat (n = 91)**			**Subject of health threat (n = 79)**		
		Vaccinated n=92, n (%)	**Not vaccinated n=61, n (%)**	***p***	**Vaccinated n=80, n (%)**	**Not vaccinated n=79, n (%)**	***p***	**Side-effects perceived n=28, n (%)**	**No side-effects perceived n=63, n (%)**	***p***	**Side-effects perceived n=26, n (%)**	**No side-effects perceived n=53, n (%)**	***p***
Parent gender	Female	55 (61.1)	35 (38.9)	.78	52 (56.5)	40 (43.5)	.07	16 (29.1)	39 (70.9)	.67	16 (31.4)	35 (68.6)	.69
	Male	37 (58.7)	26 (41.3)		28 (41.8)	39 (58.2)		12 (33.3)	24 (66.7)		10 (35.7)	18 (64.3)	
Parent age	35+	47 (55.3)	38 (44.7)	.17	44 (47.8)	48 (52.2)	.46	9 (19.6)	37 (80.4)	.02*	13 (30.2)	30 (69.8)	.58
	18-34	45 (66.2)	23 (33.8)		36 (53.7)	31 (46.3)		19 (42.2)	26 (57.8)		13 (36.1)	23 (63.9)	
Parent employment	Working	66 (59.5)	45 (40.5)	.78	62 (48.4)	66 (51.6)	.34	22 (33.8)	43 (66.2)	.32	22 (36.1)	39 (63.9)	.39
	Not working	26 (61.9)	16 (38.1)		18 (58.1)	13 (41.9)		6 (23.1)	20 (76.9)		4 (22.2)	14 (77.8)	
Total household income before tax and other deductions	≥£30,000	54 (53.5)	47 (46.5)	.01*	47 (53.4)	41 (46.6)	.41	16 (30.2)	37 (69.8)	.9	17 (36.2)	30 (63.8)	.72
	Under £30,000	35 (76.1)	11 (23.9)		26 (46.4)	30 (53.6)		11 (31.4)	24 (68.6)		8 (32.0)	17 (68.0)	
Parent highest educational or professional qualification	Degree or higher (Bachelors, Masters, PhD)	50 (58.8)	35 (41.2)	.63	43 (53.8)	37 (46.3)	.58	18 (36.7)	31 (63.3)	.18	16 (37.2)	27 (62.8)	.37
	GCSE/vocational/A-level/No formal qualifications	42 (62.7)	25 (37.3)		37 (49.3)	38 (50.7)		10 (23.8)	32 (76.2)		10 (27.8)	26 (72.2)	
Parent ethnicity	Black and Minority	5 (41.7)	7 (58.3)	.22	9 (69.2)	4 (30.8)	.25	3 (75.0)	1 (25.0)	.09	3 (33.3)	6 (66.7)	1.00
	White	87 (62.6)	52 (37.4)		69 (48.3)	74 (51.7)		25 (28.7)	62 (71.3)		23 (33.8)	45 (66.2)	
Parent chronic illness	Present	35 (64.8)	19 (35.2)	.38	26 (57.8)	19 (42.2)	.22	11 (32.4)	23 (67.6)	.80	11 (44.0)	14 (56.0)	.17
	None	57 (57.6)	42 (42.4)		53 (46.9)	60 (53.1)		17 (29.8)	40 (70.2)		15 (28.3)	38 (71.7)	
Child gender	Female	52 (62.7)	31 (37.3)	.49	37 (51.4)	35 (48.6)	.81	12 (23.5)	39 (76.5)	.09	10 (27.0)	27 (73.0)	.30
	Male	40 (57.1)	30 (42.9)		43 (49.4)	44 (50.6)		16 (40.0)	24 (60.0)		16 (38.1)	26 (61.9)	

First-born child	Yes No	50 (63.3) 42 (56.8)	29 (36.7) 32 (43.2)	.41	48 (55.2) 32 (44.4)	39 (44.8) 40 (55.6)	.18	18 (36.0) 10 (24.4)	32 (54.0) 31 (75.6)	.23	18 (37.5) 8 (25.8)	30 (62.5) 23 (74.2)	.28
Child age	Range 2 to 7 years	N=92, M=4.55, SD=1.77	N=61, M=4.62, SD=1.64	.81	N=80, M=4.30, SD=1.82	N=79, M=4.41, SD=1.64	.70	N=28, M=4.50, SD=1.84	N=63, M=4.56, SD=1.76	.89	N=26, M=4.08, SD=1.96	N=53, M=4.36, SD=1.74	.52
Child chronic illness	Present None	18 (66.7) 74 (59.2)	9 (33.3) 51 (40.8)	.47	14 (51.9) 65 (49.6)	13 (48.1) 66 (50.4)	.83	6 (33.3) 22 (30.1)	12 (66.7) 51 (69.9)	.79	8 (57.1) 18 (28.1)	6 (42.9) 46 (71.9)	.04*

*$p \leq .05$

5.2.6.2 *Vaccine uptake in 2015/16*

5.2.6.2.1 Source of the health threat

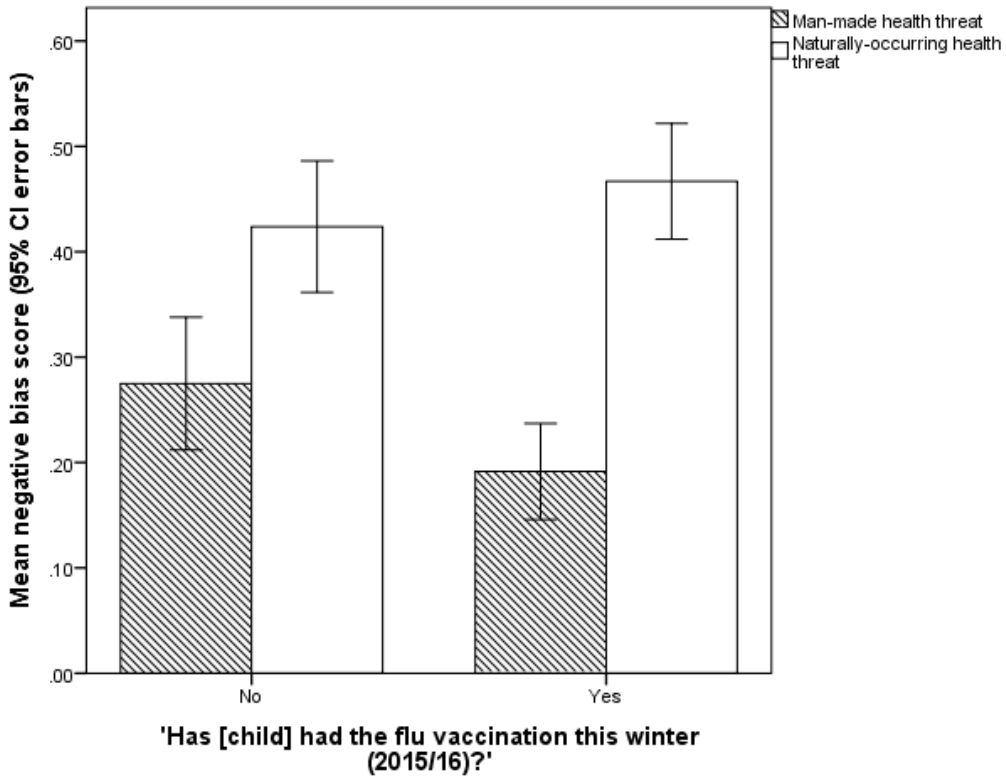
Of parents who completed items pertaining to the source of health threat, 92 had vaccinated their child for influenza in the 2015/16 influenza season and 61 had not. Mean bias scores are shown in Table 13.

There was a group difference between those who did and did not vaccinate their child for household income (see Table 12). Therefore, household income was entered into the model as a covariate. There was a significant main effect of source of health threat ($F(1,144)=16.46$, $p<.001$, $\eta_p^2=.10$) reflecting higher negative bias for naturally-occurring (M=0.45, SD=0.26) than man-made threats (M=0.22, SD=0.23). This was qualified by a significant interaction between vaccination status and source of health threat ($F(1,144)=5.22$, $p=.02$, $\eta_p^2=.04$; see Figure 6). Within-group contrasts revealed that there was a significantly bigger difference between bias for naturally-occurring health threats and man-made health threats in parents who had vaccinated (mean difference=-.28, 95% CI [-.34 to -.22], $t(91)=-9.09$, $p<.001$, $d=-0.95$) than in parents who had not vaccinated (mean difference=-.15, 95% CI [-.24 to -.06], $t(60)=-3.44$, $p=.001$, $d=-.44$). There was no main effect of vaccine uptake on bias scores ($F(1,144)=0.65$, $p=.42$, $\eta_p^2=.01$).

Table 13. Mean negative interpretation bias scores (95% CI) for source of the health risk and subject of the health risk by vaccine uptake and side-effect perception

	Influenza vaccine uptake in 2015/16		**Side-effects perceived**	
	Vaccinated n=92, mean (95% CI)	**Not vaccinated n=61, mean (95% CI)**	**Side-effects perceived n=28, mean (95% CI)**	**No side-effects perceived n=63, mean (95% CI)**
Man-made health threat	0.19 (0.15 to 0.24)	0.27 (0.21 to 0.34)	0.19 (0.11 to 0.27)	0.19 (0.13 to 0.24)
Naturally-occurring health threat	0.47 (0.41 to 0.52)	0.42 (0.36 to 0.49)	0.44 (0.33 to 0.54)	0.47 (0.41 to 0.54)
	Vaccinated n=80, mean (95% CI)	**Not vaccinated n=79, mean (95% CI)**	**Side-effects perceived n=26, mean (95% CI)**	**No side-effects perceived n=53, mean (95% CI)**
Child-relevant health threat	0.04 (0.02 to 0.07)	0.03 (0.01 to 0.05)	0.03 (0.00 to 0.07)	0.05 (0.01 to 0.09)
Self-relevant health threat	0.18 (0.14 to 0.21)	0.18 (0.13 to 0.22)	0.14 (0.08 to 0.20)	0.19 (0.14 to 0.25)

Figure 6. Mean negative interpretation bias scores with 95% CI error bars by source of health threat and vaccine uptake



5.2.6.2.2 Subject of the health threat

Of parents who completed items pertaining to the subject of health threat, 80 had vaccinated their child for influenza in the 2015/16 influenza season and 79 had not. Mean bias scores are shown in Table 13.

Participants who did and did not vaccinate their child did not differ in any personal or clinical characteristics (see Table 12). There was a main effect of subject of health threat ($F(1,157)=79.21$, $p<.001$, $\eta_p^2=.34$) indicating a higher negative bias for self-relevant (M=0.18, SD=0.19) than child-relevant (M=0.04, SD=0.12) health threats. There was no main effect of vaccine uptake ($F(1,157)=0.15$, $p=.70$, $\eta_p^2=.001$), nor was there an interaction effect ($F(1,157)=0.15$, $p=.70$, $\eta_p^2=.001$).

5.2.6.3 *Side-effect perception*

5.2.6.3.1 Source of the health threat

Of those who completed bias items pertaining to the source of the health threat and had vaccinated their child, 28 perceived side-effects while 63 did not. Mean bias scores are shown in Table 13.

Group differences were found only for parent age (see Table 12). When including parent age as a covariate, there was a main effect of source of health threat ($F(1,88)=4.05$, $p=.047$, $\eta_p^2=.04$). As previously, this reflected a higher negative bias for naturally-occurring (M=0.46, SD=0.26) than man-made (M=0.19, SD=0.22) health threats. There was no main effect of side-effect perception ($F(1,88)=0.10$, $p=.76$, $\eta_p^2=.001$), nor was there a significant interaction effect ($F(1,88)=0.16$, $p=.69$, $\eta_p^2=.002$).

5.2.6.3.2 Subject of the health threat

Of those who completed bias items pertaining to the subject of the health threat and had vaccinated their child, 26 participants perceived side-effects in their child while 53 did not. Mean bias scores are shown in Table 13.

There were group differences in the presence of a chronic illness in the child (see Table 12), which was included as a covariate. There was a main effect of subject of health threat ($F(1,75)=44.54$, $p<.001$, $\eta_p^2=.37$) with higher negative biases for

self-relevant (M=0.18, SD=0.18) than child-relevant health threats (M=0.05, SD=0.13). There was no main effect of side-effect perception ($F(1,75)=0.83$, $p=.37$, $\eta_p^2=.01$), nor was there a significant interaction effect ($F(1,75)=0.17$, $p=.90$, $\eta_p^2<.001$).

5.2.6.4 *Vaccination intention for 2016/17*

Associations between participant personal and clinical characteristics and negative interpretation bias are shown in Table 14.

5.2.6.4.1 Source of the health threat

There were group differences in bias for man-made health threats in parent gender, and in employment status for naturally-occurring health threats (see Table 14). When including parent gender and employment status as a covariate, the regression model explained 24% of the variance in bias ($R^2=.239$, $F(5,300)=18.80$, $p<.001$). Bias scores were significantly associated with vaccination intention ($\beta=-.60$, $p<.001$). Bias scores were also associated with the intention and source of health threat interaction term ($\beta=.90$, $p<.001$). To interpret the interaction, I examined the relationship between vaccination intention and negative bias for naturally-occurring and man-made health threats separately. The higher participants' intention to vaccinate, the less negatively they interpreted man-made health threats ($\beta=-.25$, $p=.002$) and the more negatively they interpreted naturally-occurring health threats ($\beta=.17$, $p=.04$; see Figure 7). There was no association between source of health threat and intention ($\beta=-.24$, $p=.19$).

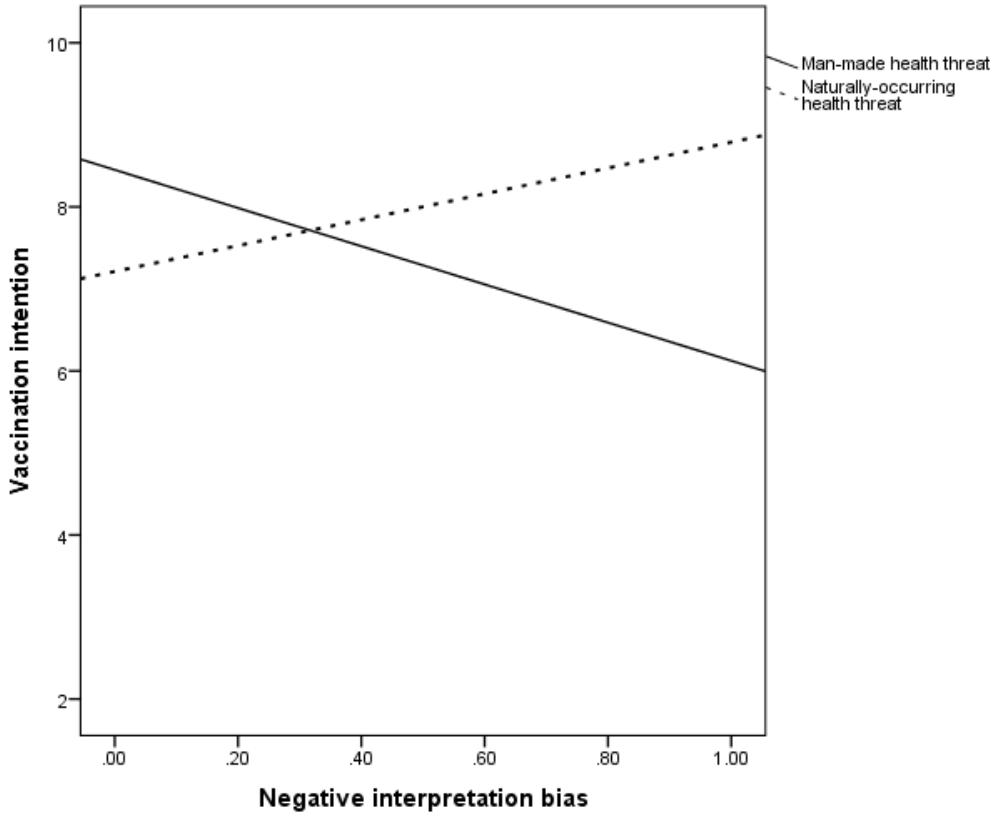
Table 14. Participant personal and clinical characteristics for those included in interpretation bias analyses and associations with negative interpretation bias

Participant characteristics	**Level**	**Source of health threat (n=158)**				**Subject of health threat (n=163)**			
		Man-made health threat		**Naturally-occurring health threat**		**Child-relevant health threat**		**Self-relevant health threat**	
		N, M, SD	***p***	**N, M, SD**	***p***	**N, M, SD**	***p***	**N, M, SD**	***p***
Parent gender	Female	N=90, M=0.26, SD=0.24	.03*	N=90, M=0.47, SD=0.25	.34	N=95, M=0.05, SD=0.12	.54	N=95, M=0.18, SD=0.18	.54
	Male	N=68, M=0.18, SD=0.23		N=68, M=0.43, SD=0.26		N=68, M=0.03, SD=0.13		N=68, M=0.16, SD=0.19	
Parent age	35+	N=89, M=0.23, SD=0.26	.89	N=89, M=0.46, SD=0.25	.81	N=94, M=0.04, SD=0.13	.88	N=94, M=0.17, SD=0.18	.72
	18-34	N=69, M=0.22, SD=0.21		N=69, M=0.44, SD=0.26		N=69, M=0.04, SD=0.11		N=69, M=0.18, SD=0.20	
Parent employment	Working	N=116, M=0.21, SD=0.22	.18	N=116, M=0.42, SD=0.26	.03*	N=131, M=0.04, SD=0.12	.85	N=131, M=0.16, SD=0.18	.03*
	Not working	N=42, M=0.27, SD=0.28		N=42, M=0.52, SD=0.24		N=32, M=0.04, SD=0.15		N=32, M=0.24, SD=0.21	
Total household income before tax and other deductions	≥£30,000	N=104, M=0.20, SD=0.23	.20	N=104, M=0.44, SD=0.26	.40	N=90, M=0.06, SD=0.14	.23	N=90, M=0.17, SD=0.18	.61
	Under <£30,000	N=47, M=0.25, SD=0.24		N=47, M=0.48, SD=0.26		N=57, M=0.03, SD=0.12		N=57, M=0.18, SD=0.21	
Parent highest educational or professional qualification	Degree or higher (Bachelors, Masters, PhD)	N=90, M=0.20, SD=0.23	.15	N=90, M=0.43, SD=0.26	.20	N=82, M=0.05, SD=0.13	.30	N=82, M=0.18, SD=0.18	.58
	GCSE/vocational/A-level/No formal qualifications	N=67, M=0.25, SD=0.24		N=67, M=0.48, SD=0.25		N=76, M=0.03, SD=0.12		N=76, M=0.17, SD=0.19	
Parent ethnicity	Black and Minority	N=12, M=0.28, SD=0.26	.36	N=12, M=0.47, SD=0.32	.84	N=13, M=0.08, SD=0.16	.29	N=13, M=0.24, SD=0.21	.16
	White	N=144, M=0.21, SD=0.23		N=144, M=0.45, SD=0.25		N=147, M=0.04, SD=0.12		N=147, M=0.17, SD=0.19	
Parent chronic illness	Present	N=57, M=0.21, 0.23	.55	N=57, M=0.49, SD=0.27	.18	N=46, M=0.05, SD=0.13	.51	N=46, M=0.21, SD=0.22	.11
	None	N=101, M=0.23, SD=0.24		N=101, M=0.43, SD=0.25		N=116, M=0.04, SD=0.12		N=116, M=0.16, SD=0.17	
Child gender	Female	N=86, M=0.20, SD=0.22	.17	N=86, M=0.46, SD=0.24	.60	N=75, M=0.05, SD=0.15	.35	N=75, M=0.18, SD=0.20	.70
	Male	N=72, M=0.25, SD=0.25		N=72, M=0.44, SD=0.27		N=88, M=0.03, SD=0.10		N=88, M=0.17, SD=0.18	
First-born child	Yes	N=81, M=0.23, SD=0.24	.92	N=81, M=0.42, SD=0.25	.08	N=89, M=0.04, SD=0.11	.63	N=89, M=0.17, SD=0.18	.65

	No	N=77, M=0.22, SD=0.23		N=77, M=0.49, SD=0.26		N=74, M=0.05, SD=0.14		N=74, M=0.18, SD=0.19	
Child age	Range 2 to 7 years	N=158, M=0.22, SD=0.24	.20	N=158, M=0.45, SD=0.25	.54	N=163, M=0.04, SD=0.12	.76	N=163, M=0.17, SD=0.19	.79
Child chronic illness	Present	N=28, M=0.24, SD=0.25	.63	N=28, M=0.44, SD=0.25	.77	N=28, M=0.11, SD=0.20	.06	N=28, M=0.16, SD=0.23	.73
	None	N=129, M=0.22, SD=0.23		N=129, M=0.45, SD=0.26		N=134, M=0.03, SD=0.10		N=134, M=0.18, SD=0.18	

*$p \leq .05$

Figure 7. Association between negative interpretation bias and vaccination intention for 2016/17 by source of health threat



5.2.6.4.2 Subject of the health threat

There were no group differences in demographics in bias for child-relevant health threats, while for self-relevant health threats there were group differences only for employment status (see Table 14). When including employment status as a covariate, the regression model explained 16% of the variance in bias (R^2=.155, F(4,297)=13.42, p<.001). There was an association between subject of the health threat and bias score (β=-.40, p=.013), reflecting a higher negative bias for self-relevant (M=0.17, SD=0.19) than child-relevant content (M=0.04, SD=0.12). There was no association between bias score and vaccination intention (β=.05, p=.75), nor was there an association between the between bias score and the intention and subject of health threat interaction term (β=.03, p=.91).

5.3 Discussion

In this study, I observed similar child influenza vaccine uptake rates (52.8%) as national estimates (52). However, over 70% of participants reported intending to

vaccinate their child in the 2016/17 influenza season. Rather than reflecting a sudden increase in uptake between the two influenza seasons, this difference probably reflects the gap between intentions and behaviours that is commonly observed across many health behaviours (417).

The largest effect exerted by any factor on uptake was that of having previously vaccinated the child for influenza, a common finding in the literature (93, 130, 408). Parental beliefs and attitudes were also strongly associated with uptake in 2015/16 and vaccination intention for 2016/17. Perceptions about the risk associated with influenza, including severity of influenza and the child's vulnerability, and believing the vaccine to be an effective way of reducing the risk of influenza were associated with vaccine uptake in 2015/16. This is in line with theories of uptake of health protective behaviours (87-89, 418) and other findings in the wider literature (91, 93). Factors relating to possible future adverse events caused by the vaccine, such as it causing short-term side-effects, long-term health problems and overloading the child's immune system, were associated with a decrease in the odds of vaccination, as was perceiving the vaccine to be unsafe. This is in line with results from my systematic review of factors associated with vaccine uptake in young children (Chapter 2) and other research investigating the effect of parental attitudes on vaccine uptake (135, 419). These factors were also strongly associated with intention to vaccinate the child in 2016/17.

Since conducting the cross-sectional study in Chapter 5, two other studies investigating parental beliefs and attitudes about vaccination and child influenza vaccine uptake in England have been published. The first of these investigated factors associated with parental hesitancy to vaccinate one's child for influenza in the 2014/15 season in England (420). This study found that concern about side-effects of the vaccine, the effectiveness of the vaccine, suspicions about others making money from vaccination and mistrust of healthcare services were among the most frequently cited reasons for vaccine refusal, in line with my results. The second study investigated the association between parental beliefs and attitudes towards vaccination using the 'vaccine attitudes examination' scale and uptake of the child influenza vaccine in the UK 'in the past year' (dates not specified) (421). Consistent with my findings, this study found that parents of children who

had not been vaccinated for influenza in the last twelve months had more negative attitudes than parents who did vaccinate their child; in particular parents were more worried about the unforeseen future effects of vaccination.

Of parents who vaccinated their child, 41% perceived acute side-effects, in line with clinical trial data (77, 78). Beliefs and perceptions relating to possible adverse effects from the vaccine were associated with increased odds of parental perception of side-effects. Social influences, including knowing another child who had experienced side-effects from the influenza vaccine and having friends, relatives or a health professional recommend against vaccination, were also associated with perception of side-effects. These factors may contribute to parents' expectations that their child will experience side-effects following vaccination, with this expectation becoming self-fulfilling (219, 249). Personal characteristics that may link to perceptions of a child's general vulnerability, including whether the child had a chronic illness or was first-born were also associated with parental perception of side-effects.

Observing side-effects following vaccination was associated with reduced re-vaccination intention for the 2016/17 influenza season; a result also seen in other studies (80). Interestingly, perceived severity of side-effects, but not worry about side-effects, was associated with decreased re-vaccination intention. This differs from evidence indicating that adherence to asthma medication is lower in children whose parents are more concerned about adverse effects from the medication (422).

Implementing an effective communication strategy targeting variables associated with vaccine uptake and intention presents a number of challenges. Terminology used in past communications about the influenza vaccine discusses the 'effectiveness' of vaccines (423, 424), however, this terminology was incompletely understood by participants. Given the association between perceived efficacy and uptake, research on how best to communicate about efficacy should now be a priority. Terminology surrounding the incidence of side-effects from vaccination used in past communications (73, 425) also gave rise to elevated estimates of incidence. In my study, median estimates of side-effects were higher than those described in the patient information leaflet for three out of

four verbal descriptors of risk ('common,' 'uncommon,' and 'very rare;' not 'very common') (73). Previous research has shown that verbal descriptors of risk often result in elevated estimates of incidence (402, 403). Additional research on how best to communicate this information is required.

My interpretation bias analyses indicated that parents tended to interpret health threats associated with natural causes, such as germs and bacteria, more negatively than health threats that were man-made, such as vaccines and other medicines. This is surprising considering the wealth of research indicating that fears about modern health are prevalent in the general population (278-281) and that unnatural, man-made health risks are perceived more negatively than naturally-occurring health risks (195, 196). The more benign interpretation of man-made health threats in my study may be due to the items used in the study. Man-made health threat items referred to medicines, vaccines, and mobile phones. Had items referenced other man-made health threats, such as radiation or nuclear waste, interpretations would likely have been more negative. My results indicate that it is important to remember that naturally-occurring health threats are also appraised negatively.

I observed no overall differences in interpretation bias between those who did and did not vaccinate their child, however there was a significant interaction effect between vaccine uptake and source of the health threat. Parents who vaccinated their child in 2015/16 interpreted naturally-occurring health threats, such as influenza, more negatively, and man-made health threats, such as vaccination, less negatively than parents who did not vaccinate their child. There was also a significant interaction between source of the health threat and vaccination intention, with those who interpreted man-made health threats more positively and naturally-occurring health threats more negatively being more likely to intend to vaccinate their child in 2016/17. These results appear logical: a greater tendency to consider man-made vaccination as less threatening and the naturally-occurring influenza virus as more threatening should translate into a greater willingness to use the vaccination. As no other studies have investigated the association between cognitive biases and child vaccination, I cannot state whether my findings are in line with the results of others, however the convergent nature of findings from these two outcome measures lends confidence to my results.

Results from the most closely related study I have found, investigating attention biases in asthma medication adherence, lend support to the notion that information processing biases are associated with uptake of medication (208).

Relating these findings to the wider vaccination literature, underlying differences in cognitive biases may affect child vaccination uptake through the higher-level, conscious appraisal of health threats. For example, associations between vaccine uptake and intention and interpretation bias pertaining to the source of the health threat map on to factors associated with vaccine refusal in my systematic review (Chapter 2). Specifically, a more negative interpretation of man-made health threats potentially may be reflected in the belief that the vaccine can cause adverse effects, while less negative interpretations of naturally-occurring health threats may be reflected in a more benign appraisal of influenza. The health belief model, the theory of planned behaviour, the protection motivation theory and the health action process approach all postulate that perceived risks of a behaviour influence the uptake of health behaviours (87-89, 418). My results indicate threat appraisal may be biased at a more basic level: information processing.

Parents also consistently interpreted threats to their own health more negatively than threats to their child's health. Interpreting threats to oneself more negatively than threats to others is a common finding in the interpretation bias literature (e.g. (426)), with previous research indicating that parental interpretation biases for physical threats are stronger in self-relevant situations than child-relevant situations (198, 199). This is in spite of the fact that when asked, parents tend to claim that the risk of their child becoming ill is more important than the risk of themselves becoming ill (92). The use of strict task parameters such as a time limit in which to complete task materials and being under cognitive load, may have reduced parents' ability to complete task materials in a socially desirable manner (410). I found no evidence for associations between parental interpretation biases pertaining to the subject of the health threat and child influenza vaccination in 2015/16 or vaccination intention for 2016/17.

With relation to perception of side-effects from the child influenza vaccination, I found no evidence for an association with interpretation bias pertaining to either the source or the subject of the health threat. These findings differ from results of

another study in which mothers of children with chronic abdominal pain tended to interpret ambiguous facial stimuli as being painful (385). The use of ambiguous scenarios in my study, as opposed to ambiguous images, might explain this difference in findings. Pictorial stimuli are more aversive than verbal stimuli (427) and thus potentially invoke a stronger emotional response, causing more biased processing. In addition, only those who had vaccinated their child were included in the side-effect perception analyses. This subset of parents may have had more similar patterns of interpretation biases, meaning that differences between parents who did and did not perceive side-effects were more difficult to detect.

5.3.1 Limitations

Although the study included a large, demographically representative cross-section of parents, several limitations need to be considered. One limitation is its cross-sectional design, making causal inferences difficult to draw for some of the associations observed. This is particularly problematic with respect to the association between beliefs and attitudes and side-effect reporting. While it is possible that negative beliefs and attitudes towards the vaccine lead to an increased likelihood of side-effects being observed, it is also possible that observing side-effects leads to negative beliefs and attitudes. Similarly, I was unable to demonstrate causality between interpretation biases and vaccination behaviour. To disentangle the direction of causality, a longitudinal study should be conducted.

A second limitation relates to selection bias. Whether members of market research panels are psychologically representative of the general population in terms of beliefs and attitudes to vaccination is unknown (428). While it is possible that parents who had vaccinated their child were more likely to be generally ‘compliant’ or publicly spirited and hence complete the study, rates of reported uptake were in line with national figures (52). Although quotas were used to ensure a nationally representative sample, it should be noted that parent gender was not split equally in the study; this is likely due to the uneven split in parent gender in those registered in the National Readership Survey which formed the basis for my quotas (405). In interpretation bias analyses, as participants assigned to receive bias items pertaining to the source and the subject

of the health threat and those included and excluded from analyses differed in their personal and clinical characteristics, those included in the analyses were no longer representative of the general population of parents of vaccine-eligible children in the UK.

Third, the response rate for this study was low. However, such response rates are common in market research (e.g. (272, 429)) and evidence indicates that resulting estimates of health-related outcome variables are accurate (429).

Fourth, group sizes differed for analyses pertaining to vaccine uptake, side-effect perception and vaccination intention. In interpretation bias analyses, personal and clinical characteristics controlled for also differed. However, due to the innovative nature of the interpretation bias research and smaller sample sizes included in analyses, controlling for all personal and clinical characteristics was considered too conservative.

Fifth, while the scrambled sentence task is usually completed in person under the supervision of the researcher, participants in this study completed the task remotely. Although this enabled many participants to complete materials in a short space of time, only approximately one-third of participants completed the task to the standard necessary for inclusion in the analysis. While sample sizes were still large and I was well powered to detect medium effect sizes in interpretation bias analyses, it is possible that I failed to detect small, yet relevant effects.

Sixth, while the scrambled sentences task measures interpretation bias, no task can measure only one single information processing system. Consequently, there is a chance that participants' attention biases could have affected scrambled sentence task results, with negatively biased participants attending more to the negative, rather than positive, words which made up items. In spite of this, the scrambled sentence task remains a widely-used and valid measure of interpretation bias.

Lastly, multiple analyses were run on the data, increasing the risk of Type I errors.

5.3.2 Conclusions

This study was the first to investigate parental beliefs and attitudes towards the newly introduced child influenza vaccine in the UK and the first to investigate the association between beliefs and attitudes and side-effect perception following immunisation. Although a causal link cannot definitively be established, the data are consistent with the theory that past behaviour, beliefs, attitudes and social influences affect both uptake and side-effect perception. This was the also the first study to investigate whether information processing biases were associated with child vaccination, finding evidence for an association between interpretation biases pertaining to the source of the health threat and vaccine uptake and vaccination intention. Specifically, actual and intended vaccination was associated with a tendency to interpret man-made health threats less negatively and naturally-occurring health threats more negatively. To determine whether psychological factors play a causal role in vaccine uptake, vaccination intention and parental side-effect perception, longitudinal research is required.

Chapter 6. Prospective cohort study

In my cross-sectional study (Chapter 5), I found good evidence that parental beliefs and attitudes about influenza and the child influenza vaccine were associated with child influenza vaccination and perception of side-effects from vaccination. Parental interpretation biases pertaining to the source of the health threat were also associated with vaccination. Parents who perceived side-effects from vaccination were less likely to intend to re-vaccinate their child the following year than those who did not perceive vaccine side-effects. However, the cross-sectional nature of the study limited my interpretation of the results. First, I was unable to make causal inferences about the nature of associations between beliefs and attitudes, interpretation biases and vaccination behaviour. For example, it is entirely plausible that having perceived side-effects following vaccination might alter parental beliefs and attitudes towards vaccination. Second, I was unable to measure vaccination rates in the 2016/17 influenza season to identify whether parental vaccination intention for 2016/17 was associated with actual vaccination in 2016/17. Third, I was unable to measure some variables of interest. Most notably, I was not able to assess expectations, which play a central role in the nocebo phenomenon (214, 218, 219). In Chapter 4, I hypothesised that parental perception of side-effects from the child influenza vaccine would be associated with: pre-existing symptoms in the child; parental expectation that the child would develop side-effects; negative beliefs about medications; parental perception that the child was sensitive to medicines; modern health worries; more benign beliefs about influenza and more negative beliefs and attitudes about the vaccine; negative psychological traits; negative interpretation biases; and parent and child personal and clinical characteristics (Hypothesis 4.3.1 to Hypothesis 4.3.6).

While side-effects from the child influenza vaccine tend to occur on the day of vaccination (74) and are mostly ‘mild in nature and short term’ (73), parents decide whether to re-vaccinate their child for influenza one year after their initial vaccination. Parents who remember that their child experienced side-effects from the vaccine in the previous year might be less likely to re-vaccinate their child.

However, symptom recall is often inaccurate, and is influenced by environmental factors, symptom expectation, previous symptom experiences from the exposure and symptom severity (234). Thus, it is important to identify psychological factors associated with both side-effect perception and side-effect recall. I measured parental perception of side-effect three days and one month after their child's vaccination.

Parental perception of side-effects may also affect how sensitive parents believe their child to be to medicines and how much parents trust healthcare workers such as those delivering vaccination. Therefore, I also used this study to investigate whether parental perception of side-effects negatively affected parents' perception of their child's sensitivity to medicines and parental trust in healthcare workers.

While there is much research investigating why parents initially choose to accept or refuse vaccination for their child, there are no publicly available data on re-vaccination rates for the child influenza vaccine or analyses investigating why parents who vaccinate their child for influenza in one year, choose not to do so in a subsequent year. In addition to perception of side-effects from the initial vaccination and associated worry, other factors which may change between a parent's initial vaccination decision and their decision to re-vaccinate one year later may also affect re-vaccination. For example, following initial vaccination, increases in how sensitive parents believe their child to be to medicines, or decreases in their trust in healthcare workers, may be associated with later vaccine refusal (430, 431). Negative information received from healthcare workers during the initial vaccination appointment, and the interaction between information received and how much trust the parent has in the healthcare worker may also influence a parent's decision to re-vaccinate. In Chapter 4, I hypothesised that a lack of intention to re-vaccinate in 2017/18 and re-vaccination refusal in 2017/18 would be associated with: perception of side-effects from the vaccine in 2016/17; a suggestion from the healthcare worker in the 2016/17 vaccination appointment that the vaccine caused side-effects; perceiving the child to be more sensitive to medicines after vaccination in 2016/17; decreased trust in healthcare workers after vaccination in 2017/18; negative interpretation biases;

and parent and child personal and clinical characteristics (Hypothesis 4.2.1 to Hypothesis 4.2.5).

Results from my cross-sectional study indicated that interpretation biases pertaining to the subject of the health threat (self- and child-referent) were not associated with vaccination behaviour (Chapter 5). Therefore, in this study, I chose to investigate only parental interpretation biases pertaining to the source of the health threat (man-made and naturally-occurring).

For this chapter, I conducted a prospective cohort study of parents vaccinating their child for influenza in primary care practices in South London during the 2016/17 influenza season. I investigated whether psychological factors were associated with parental perception of side-effects from the influenza vaccine and re-vaccination intention for the 2017/18 influenza season. I also investigated re-vaccination rates in the 2017/18 season and psychological factors associated with re-vaccination refusal.

6.1 Method

6.1.1 Design

Participants in this prospective cohort study completed questionnaires before their child received the influenza vaccine for the 2016/17 influenza season (T1), three days after their child's vaccination (T2) and one month after their child's vaccination (T3). Re-vaccination was assessed at the end of the 2017/18 influenza season (T4).

6.1.2 Participants and recruitment

Participants were eligible for the study if they: had a child aged two to four on 31st August 2016; were eighteen years or over; and spoke fluent English.

Potential participants were identified by eleven primary care practices in South London and were sent letters informing them about the study. Parents were then approached upon arrival at the practice for their child's influenza vaccination by LS or a research nurse. Additional participants from other practices participated online.

6.1.3 Materials

Full study materials can be found in Appendix 10 (T1 questionnaire), Appendix 11 (T2 questionnaire), Appendix 12 (T3 questionnaire), Appendix 6 (scrambled sentence task) and Appendix 13 (similarity ratings task).

6.1.3.1 *Outcome measures*

I asked parents at T2 and T3 if they thought their child had 'experienced any of the following side-effects because of their latest child flu vaccine.' For my list of side-effects, I used an adapted parent-report form of the Patient Health Questionnaire (PHQ-15) (406), to which I added potential side-effects of the vaccine listed in the patient information leaflet (77), and symptoms suggested by the literature (246), or by parents during previous piloting. The symptom list was the same as that used in the cross-sectional study described in Chapter 5.

As in my cross-sectional study, re-vaccination intention for the 2017/18 influenza season was measured at T2 and T3 by two items adapted from Payaprom et al. (407) ('I **want** [child] to be vaccinated for flu next year' and 'I **intend** [child] to be vaccinated for flu next year') which were rated on a five-point Likert scale from 'strongly disagree' to 'strongly agree.'

Re-vaccination in the 2017/18 influenza season was ascertained where possible by accessing vaccination records from the primary care practice. If this was not possible, parents were contacted directly and asked if their child had been 'vaccinated in the 2017/18 flu season.' Possible answers were 'yes,' 'no,' and 'don't know.'

6.1.3.2 *Symptoms prior to vaccination*

A child's existing symptoms at the time of vaccination were measured by asking parents if their child had 'shown signs of any of the following symptoms in the last 24 hours.' The list of symptoms provided was the same as that used in my outcome measure for reporting side-effects perceived.

6.1.3.3 *Expectation*

A single direct measure of expectation asked parents how likely it was that their child would 'get short term side-effects from the flu vaccine' on a five-point Likert scale of 'very unlikely' to 'very likely.' Parents were also asked how likely

five different sources (friends and family, official websites and departments, the media, the NHS influenza vaccination leaflet, and the healthcare worker) had said side-effects were from the vaccine on a four-point Likert scale from ‘very likely’ to ‘very unlikely.’ Parents were asked to what extent they agreed that these sources of information could be trusted on a five-point Likert scale from ‘strongly agree’ to ‘strongly disagree.’ Parents were also asked whether they knew ‘any children who have experienced side-effects from the flu vaccine,’ with possible answers of ‘yes, several other children,’ ‘yes, one other child,’ and ‘no, I don’t know any children who had side-effects from the flu vaccine.’ All expectation questions were asked at T1 apart from those relating to the suggestion of side-effects from the heath care worker as these could not be asked until after the vaccination appointment had taken place, at T2.

6.1.3.4 *Symptoms following previous vaccinations*

At T1, parents were asked if the child had ‘ever had side-effects’ from previous influenza vaccinations and other routine vaccinations. Parents who indicated their child had experienced side-effects from previous influenza vaccinations were asked how severe the side-effects were on a five-point Likert scale of ‘very mild’ to ‘very severe’ and how worried they had been about the side-effects on a four-point Likert scale from ‘not at all worried’ to ‘very worried.’ Parents who indicated their child had experienced side-effects from other routine childhood vaccinations were asked how worried they had been.

6.1.3.5 *Psychological traits*

Participants completed four personality measures at T2. Trait anxiety was measured by the short form of the State-Trait Anxiety Inventory (STAI-T) (432). Trait affect was measured using the short form Positive and Negative Affect Schedule (PANAS) (433). Neuroticism was measured using the neuroticism items from an abbreviated form of the Eysenck Personality Questionnaire – Revised (EPQR-A) (434). Optimism and pessimism were measured using the revised Life Orientation Test (LOT-R) (294).

6.1.3.6 *Beliefs about medicines and other technologies*

Participants' perception of their child's sensitivity to medicines was measured at both T1 and T3 using an adapted parental report version of the Perceived Sensitivity to Medicines questionnaire (PSM) (275).

The Modern Health Worries Questionnaire (MHW) (278) and the Beliefs about Medicines Questionnaire, general section (BMQ-G) (435) were both completed at T2.

6.1.3.7 *Beliefs and attitudes about influenza and the child influenza vaccine*

Beliefs and attitudes towards influenza and the child influenza vaccine were measured by a series of fifteen statements. Belief and attitude statements were the same as those used in the cross-sectional study in Chapter 5; only those that significantly associated with vaccination uptake or perception of side-effects in the cross-sectional study were selected for use in the current study. Parents indicated how much they agreed with belief and attitude statements on a five-point Likert scale from 'strongly agree' to 'strongly disagree.' Beliefs and attitudes were measured at T1, apart from statements relating to how serious parents thought influenza would be for the child, themselves and other people in the child's household, which were measured at T2. At T2, parents were also asked how much it would impact their daily life if their child were to catch influenza on a four-point Likert scale from 'not at all' to 'a great extent.'

6.1.3.8 *Trust in healthcare workers*

Participants' trust in healthcare workers was measured at both T1 and T3 using an adapted form of the Meyer Credibility Scale (MCS) (436).

6.1.3.9 *Interpretation bias*

As I found no evidence for associations between vaccination behaviour and parental interpretation biases pertaining to the subject of the health threat (self- and child-referent) (Chapter 5), I only investigated parental interpretation biases pertaining to the source of the health threat (man-made and naturally-occurring) in this study.

Two tasks were used to measure interpretation bias; the scrambled sentence task (411) and the similarity ratings task.

6.1.3.9.1 Scrambled sentence task

The scrambled sentence task consisted of ten items. Items were the same as those used in the cross-sectional study for the source of the health threat (Chapter 5), except for four items which yielded multiple responses which were similarly endorsed and thus were replaced (see Appendix 6 for full item list). Man-made health threats included vaccines, household cleaning products, medicines, side-effects and mobile phones (five items), while naturally-occurring health threats included influenza, illnesses, bacteria, wild plants and getting a sun-tan (five items). Items consisted of six words presented in a fixed-random order which could be unscrambled to create a meaningful five-word statement which was either positive or negative. Items were presented in a fixed-random order. Bias scores were calculated by dividing the number of negative statements produced by a participant by the total number of items attempted. Higher bias scores indicate higher negative interpretation bias.

Participants completed the scrambled sentence task under cognitive load, which increases the sensitivity of the task by stopping strategic inhibition of biases (411). Before unscrambling the sentences, participants were asked to learn a six-digit number. After unscrambling the sentences, participants were asked to recall the number and indicated whether they used any memory aides, such as writing the number down, to help them recall the number. The task was also completed under timed conditions, with participants having two minutes in which to complete the ten items.

6.1.3.9.2 Similarity ratings task

Participants also completed a similarity ratings task, however due to the small number of parents who completed the similarity ratings task and resulting lack of power, I was unable to draw any conclusions from these results. For completeness, I have reported the methods and results of the similarity ratings task in Appendix 14.

6.1.3.10 *Personal and clinical characteristics*

Participants were asked for their age and gender. Personal characteristics relating to the index child included age, gender and whether they were the parent's first child. I also asked about clinical characteristics, such as whether the parent or

child had a long-term health condition and whether there were any people 'at risk' for influenza in the child's household. Participants were asked whether the child was up-to-date for other routine vaccines.

6.1.4 Piloting

Questionnaire materials were piloted with three parents of children aged two to four years for understanding; items were reworded if necessary, except where items came from a published scale.

6.1.5 Procedure

Ethical approval for the study was granted by the NHS Research Ethics Committee (Reference: IRAS ID: 192325, REC reference: 16/LO/1003).

Participants were recruited into the study between 1st October 2016 and 16th December 2016. Prior to completing T1 materials, consent was obtained from all parents following standard practice from my research ethics committee.

A summary of measures included at each time point of the study is shown in Table 15. Parents completed T1 materials in the waiting room at the primary care practice immediately prior to their child's vaccination appointment, or online before their child's vaccination appointment. One item in T1, asking whether the child had experienced any symptoms in the past 24 hours, was excluded from the online version; participants were contacted on the day of their child's vaccination appointment to answer this.

Three days after the vaccination appointment, parents were contacted via email with a link to the T2 materials, which were available online. If participants did not have access to email, T2 materials were completed by telephone. The scrambled sentence task was included as part of T2 materials. All interpretation bias materials were completed online; those completing T2 task materials by telephone did not complete the scrambled sentence task. At the end of the T2 questionnaire I asked parents for consent to access their child's vaccination records for the 2017/18 season through the primary care practice.

One month after the vaccination appointment, parents were emailed a link to T3 task materials. If participants did not have access to email, T3 materials were completed by telephone.

Re-vaccination status was collected at the end of the 2017/18 influenza season (T4). After the end of vaccination at each primary care practice, vaccination records were accessed for children of parents who had given consent. For those who had not consented to me accessing the child's vaccination records, or whose records were unable to be accessed, I contacted parents via email or telephone. All parents of children who were of age to receive the vaccine at school were contacted directly.

Table 15. Summary of measures included at each time point of the prospective cohort study

Time point	Predictor	Measure	Mode of completion
T1 (before vaccination)	Expectation (direct measure)	Likelihood of child getting 'short-term side-effects from the flu vaccine'	Waiting room of primary care practice/online
	Expectation (source of suggestion of symptoms)	Trust in sources of information (friends/family/relatives; official websites; media; NHS influenza vaccination leaflet); suggestion of side-effects from sources of information (friends/family/relatives; official websites; media; NHS influenza vaccination leaflet)	
	Expectation (social observation)	Knowing another child who had side-effects from the child influenza vaccine; severity of side-effects	
	Beliefs about medicines and other technologies	Adapted parental report form of perceived sensitivity to medicines scale	
	Trust in healthcare workers	Meyer Credibility Scale	
	Beliefs and attitudes about influenza and the child influenza vaccine	Beliefs and attitudes about influenza and the child influenza vaccine	
	Symptoms following previous vaccinations (influenza vaccine)	Previous side-effects from the child influenza vaccine; severity of side-effects; and worry about side-effects perceived	
	Symptoms following previous vaccinations (other routine vaccines)	Previous side-effects from other routine vaccines; and worry about side-effects perceived	
	Symptoms prior to vaccination	Pre-existing symptoms in the child*	
	Personal and clinical characteristics	Child gender; child age; relationship to child; previous child influenza vaccination	
T2 (three days after vaccination)†	Outcome measure (side-effect perception)	Side-effect perception; severity of side-effects perceived; and worry about side-effects	Online/telephone
	Outcome measure (re-vaccination intention)	Re-vaccination intention	
	Expectation (source of suggestion of symptoms)	Trust in healthcare worker as a source of information; suggestion of side-effects from healthcare worker in vaccination appointment	
	Beliefs and attitudes about influenza and the child influenza vaccine	Influenza would be a serious illness for child/oneself/someone in child's household; impact on daily life if child were to catch influenza	
	Beliefs about medicines and other technologies	Beliefs about medicines questionnaire – general section; modern health worries	

	Psychological traits	State-Trait Anxiety Inventory (STAI-T); abbreviated form of the Eysenck Personality Questionnaire – Revised (EPQR-A); Positive and Negative Affect Schedule (PANAS); revised Life Orientation Test (LOT-R)	
	Interpretation bias	Scrambled sentence task‡	
	Personal and clinical characteristics	Other 'at risk' people in household; first child; parent chronic illness; child chronic illness; child up-to-date on other routine vaccines; parent age; parent gender	
T3 (one month after vaccination)†	Outcome measure (side-effect perception)	Side-effect perception; severity of side-effects perceived; and worry about side-effects	Online/telephone
	Outcome measure (re-vaccination intention)	Re-vaccination intention	
	Beliefs about medicines and other technologies	Adapted parental report form of perceived sensitivity to medicines scale	
	Trust in healthcare workers	Meyer Credibility Scale	
T4 (end of the 2017/18 influenza season)	Re-vaccination	Re-vaccination in 2017/18 influenza season	Vaccine records/ email/telephone

* Participants who completed T1 materials online were not asked this question as part of T1 as materials could be completed at any time before vaccination. Instead, they were contacted on the day of their child's vaccination to answer this item.

† For those completing T2 and T3 materials online, after completing T2 and T3, participants were asked if they wanted to complete an additional task: the similarity ratings task.

‡ Participants who completed T2 materials by telephone did not complete the scrambled sentence task; only participants completing T2 online completed the scrambled sentence task.

6.1.6 Power

I used G*Power (414) to run a sample size calculation based on the ability to detect a small odds ratio of 1.6 (437) for symptom perception between parents with high and low expectation of symptoms. Clinical trial data suggested that 47.9% of children who received the Fluenz tetra vaccine experienced side-effects (77). Survey data suggested that I could assume equal sample sizes between those who did and did not expect symptoms (408). To detect this difference as significant at the 5% level with 85% power required a total sample size of 180. I therefore aimed to recruit 300 people at T1, to allow for a 40% attrition rate.

Only a subset of survey participants completed interpretation bias materials to a satisfactory level and were included in the analyses presented here. I ran post-hoc power analyses for each of the interpretation bias analyses. For the cross-sectional tests (side-effect perception at T2 and re-vaccination intention for 2017/18), I based power analyses on the use of a repeated measures ANOVA. Using a-priori parameters of two groups and two measures, with the correlation between measures being 0.5 and an alpha of .05 I had 98.9% power to detect medium effect size (f=0.25) for a within-between interaction in the side-effect perception analyses (n=74) and 99.0% power for the re-vaccination intention analyses (n=75).

For the longitudinal tests (side-effect perception at T3 and actual re-vaccination in 2017/18), I based power analyses on the use of logistic regression analyses. Using a-priori parameters of a two-tailed test, I had 77.6% power to detect medium size effects (OR=2.5) in the side-effect perception analyses (n=66) and 81.5% power in the re-vaccination for 2017/18 analyses (n=72).

6.1.7 Protocol registration

The protocol for the study was registered in advance on clinicaltrials.gov (identifier: NCT02909855).

6.1.8 Analysis

6.1.8.1 *Predictors of side-effect report*

I recoded report of a symptom at T2, T3 or in the 24 hours prior to vaccination into three binary variables (reported at least one symptom at the relevant time point versus no symptoms reported).

I recoded data where parents indicated that they had not received information from a particular source as missing. A composite measure of symptom suggestion from each information source was created by multiplying the suggestion of side-effects from that source by the participant's trust in that source. I treated knowing another child who had experienced side-effects following vaccination for influenza as a binary variable (yes or no). General beliefs and attitude questions were recoded to binary variables (agree or disagree); as in the cross-sectional study, I treated 'neither agree nor disagree' as missing data (Chapter 5).

I used separate binary logistic regressions to determine whether perception of side-effects at T2 and T3 were associated with: pre-existing symptoms; expectation for the child to develop side-effects; previous experience of side-effects; personality traits; beliefs about medicines and other technologies; beliefs and attitudes about influenza and the child vaccine; and personal and clinical characteristics. Multivariate logistic regressions were used to calculate the same associations adjusting for personal characteristics. For predictors of side-effect report, re-vaccination intention for 2017/18 and re-vaccination in 2017/18, only results of multivariate analyses are reported narratively; results of univariate analyses are shown in the tables. In addition, where analyses relied on under ten participants in one cell, these are not reported narratively unless they have a material impact on results.

6.1.8.2 *Expectations as a mediating variable*

I ran zero-order correlations to identify factors that were correlated with direct expectations of the child developing side-effects and side-effect report at T2 and T3. Factors that were correlated with both direct expectations and side-effect report at either T2 or T3 were entered into mediation analyses using the method described by Mackinnon (438). I ran mediation using standardised coefficients to see whether the report of side-effects was mediated by expectation. I computed

bias-corrected 95% confidence intervals using bootstrapping (2000 repetitions). I entered personal and clinical characteristics into the model as covariates.

6.1.8.3 *Predictors of re-vaccination intention for 2017/18*

I dichotomised answers to re-vaccination intention questions, with participants coded as 'definitely intending' to re-vaccinate their child (answered 'agree' or 'strongly agree' to both questions) or 'not definitely intending' to re-vaccinate (answered 'neither agree nor disagree,' 'disagree' or 'strongly disagree' to one or both questions). I then used intention at both T2 and T3 to create a single overall intention score. Where participants only completed one follow-up questionnaire I used the data available to me to classify their response as either 'definitely intend' or 'do not definitely intend' to re-vaccinate. Where participants completed both T2 and T3 and had concordant intentions, I classified them as either 'definitely intend' or 'do not definitely intend' as appropriate. If conflicting intentions were given at T2 and T3 I classified participants as 'do not definitely intend.'

I computed the difference between perceived sensitivity to medicines at T3 and T1 by subtracting T1 scores from T3. I computed the difference between trust in healthcare workers at T3 and T1 by subtracting scores from T1 from T3.

I used binary logistic regression analyses to identify whether re-vaccination intention for 2017/18 was associated with: report of a side-effect at T2 or T3; perceived severity and worry about side-effects; suggestion that the child would experience side-effects by a healthcare worker; the combined score for suggestion that the child would experience side-effects and trust in the healthcare worker; changes in the parents' perception of how sensitive the child was to medicines following vaccination in 2016/17; changes in trust in healthcare workers following vaccination in 2016/17; and personal and clinical characteristics. Multivariate logistic regressions were used to calculate the same associations adjusting for personal characteristics. Re-vaccination intention was coded positively, with an odds ratio greater than one indicating increased odds of definitely intending to re-vaccinate.

6.1.8.4 *Predictors of re-vaccination in 2017/18*

I coded re-vaccination status in the 2017/18 influenza season into a binary variable (re-vaccinated or not re-vaccinated). I coded data where parents indicated they were not sure if their child had been re-vaccinated as missing data.

I used binary logistic regression analyses to identify whether not re-vaccinating one's child in the 2017/18 influenza season was associated with: report of a side-effect at T2 or T3; perceived severity of and worry about side-effects; suggestion that the child would experience side-effects by a healthcare worker; the combined score for suggestion that the child would experience side-effects and trust in the healthcare worker; changes in the parents' perception of how sensitive the child was to medicines following vaccination in 2016/17; changes in trust in healthcare workers following vaccination in 2016/17; and personal and clinical characteristics. Multivariate logistic regressions were used to calculate the same associations adjusting for personal characteristics. Re-vaccination was inversely coded, with an odds ratio greater than one indicating increased odds of re-vaccination refusal.

6.1.8.5 *Predictors of change in perceived sensitivity*

I used a paired samples t-test to see if parents' perception of their child's sensitivity to medicines had changed from T1 to T3. I used linear regression analyses to identify whether reporting side-effects at T2 or T3 was associated with an increase in perceived sensitivity to medicines. For these analyses, I controlled for perceived sensitivity to medicines at T1 (439).

6.1.8.6 *Predictors of change in trust in healthcare workers*

I used a paired samples t-test to see if parents' trust in healthcare workers had changed from T1 to T3. I used linear regression analyses to identify whether reporting side-effects at T2 or T3 was associated with a decrease in trust in healthcare workers. For these analyses, I controlled for trust in healthcare workers at T1 (439).

6.1.8.7 *Sensitivity analyses*

I ran sensitivity analyses to identify whether clustering by primary care practice affected the significance of any of the results. Primary care practice was used as a

proxy for socio-economic factors. I used mixed models, including primary care practice as a random effect in the regressions. For mediation analyses, I followed the same approach to see if clustering affected pathways.

Analyses controlled for all personal and clinical characteristics apart from whether the child was up-to-date with other routine vaccinations.

6.1.8.8 *Interpretation bias*

I excluded participants from the interpretation bias analyses if they had more than 40% missing data for either man-made health threat items or naturally-occurring health threat items. I also excluded participants if they reported using a strategy to remember the number and therefore were not under cognitive load.

As the scrambled sentence task was included in T2 task materials, analyses with the outcomes of side-effect perception at T2 and re-vaccination intention for 2017/18 were cross-sectional, while analyses with the outcomes of side-effect perception at T3 and re-vaccination in 2017/18 were longitudinal.

To investigate whether there was an association between interpretation bias and cross-sectional outcomes (side-effect perception at T2 and re-vaccination intention for 2017/18) I ran two mixed-model, repeated measures ANOVAs. In the first, the between-participant factor was side-effect perception at T2 (side-effects perceived; no side-effects perceived), while in the second it was re-vaccination intention (intend to re-vaccinate; do not definitely intend to re-vaccinate). The within-participant factor for both ANOVAs was the source of the health threat (man-made or naturally-occurring).

To investigate whether there was an association between interpretation bias and longitudinal outcomes (side-effect perception at T3 and re-vaccination in 2017/18), I ran two hierarchical logistic regressions. In the first, the dependent variable was side-effect perception at T3 (side-effects perceived; no side-effects perceived), while in the second it was, re-vaccination in the 2017/18 influenza season (re-vaccinated; not re-vaccinated). Bias score, source of health threat (man-made or naturally-occurring) and a bias score*source of health threat interaction term were entered as the independent variables in both regression analyses.

For all interpretation bias analyses, personal and clinical characteristics (parent age, parent gender, parent chronic illness, other 'at risk' person in household, child gender, child age, first-born child and child chronic illness) were investigated to see whether there was a univariate association ($p \leq .05$) with outcome variables. As in chapter 5, where personal and clinical characteristics were associated with outcome variables, they were entered into the analyses as covariates. In regression analyses, covariates were entered into the regression model as the first block; predictor variables were entered into the model as the second block.

6.1.9 Statistical software

All analyses were run in SPSS version 22 (416), apart from mediation analyses which were run in Stata 12 (440). The binary_mediation macro was used, which allows for dichotomous outcomes as well as taking covariates into account.

6.2 **Results**

6.2.1 Participants

270 participants were recruited from fourteen primary care practices. 233 participants initiated T2 follow-up, with 202 (74.8%; 185 mothers) participants completing all items. 200 participants initiated T3 follow-up, with 195 (72.2%; 164 mothers) completing all items. 232 (85.9%; 190 mothers) participants completed T4 follow-up. 177 participants (65.6%) initiated all three follow-ups with 145 participants (53.7%) completing them all. Participants' personal characteristics can be found in Table 16.

Table 16. Parent and child personal and clinical characteristics and associations with perception of side-effects from vaccination

Participant characteristics	Level	Side-effects reported at T2				Side-effects reported at T3			
		Side-effects perceived n=98, n (%)	No side-effects perceived n=129, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Side-effects perceived n=72, n (%)	No side-effects perceived n=128, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]
Parent gender	Female	81 (43.8)	104 (56.2)	1.15 (0.58 to 2.26)	1.23 (0.47 to 3.24)	57 (34.8)	107 (65.2)	0.75 (0.36 to 1.56)	0.78 (0.28 to 2.15)
	Male	17 (40.5)	25 (59.5)	Reference	Reference	15 (41.7)	21 (58.3)	Reference	Reference
Parent age	45+	8 (50.0)	8 (50.0)	1.55 (0.50 to 4.80)	1.44 (0.43 to 4.88)	4 (30.8)	9 (69.2)	0.86 (0.23 to 3.26)	0.77 (0.19 to 3.07)
	35-44	41 (40.2)	61 (59.8)	1.04 (0.52 to 2.07)	1.01 (0.46 to 2.20)	34 (36.6)	59 (63.4)	1.11 (0.53 to 2.37)	1.07 (0.46 to 2.50)
	18-34	20 (39.2)	31 (60.8)	Reference	Reference	15 (34.1)	29 (65.9)	Reference	Reference
Parent chronic illness	Present	18 (36.7)	31 (63.3)	0.74 (0.38 to 1.43)	0.57 (0.23 to 1.42)	15 (34.1)	29 (65.9)	0.95 (0.46 to 1.94)	1.00 (0.39 to 2.56)
	None	72 (43.9)	92 (56.1)	Reference	Reference	47 (35.3)	86 (64.7)	Reference	Reference
Other 'at risk' people in child's household	Yes	33 (40.7)	48 (59.3)	0.85 (0.48 to 1.52)	0.99 (0.47 to 2.06)	23 (34.3)	44 (65.7)	0.95 (0.49 to 1.84)	0.87 (0.39 to 1.92)
	No	50 (44.6)	62 (55.4)	Reference	Reference	33 (35.5)	60 (64.5)	Reference	Reference
Child gender	Female	42 (35.9)	75 (64.1)	0.53 (0.31 to 0.90)*	0.45 (0.23 to 0.88)*	34 (34.3)	65 (65.7)	0.85 (0.48 to 1.52)	0.85 (0.41 to 1.75)
	Male	56 (51.4)	53 (48.6)		Reference	38 (38.0)	62 (62.0)		Reference
First-born child	Yes	53 (40.2)	79 (59.8)	0.78 (0.45 to 1.36)	0.78 (0.39 to 1.60)	35 (30.7)	79 (69.3)	0.73 (0.32 to 1.15)	0.91 (0.42 to 2.00)
	No	38 (46.3)	44 (53.7)	Reference	Reference	27 (42.2)	37 (57.8)	Reference	Reference
Child age	Range 1 to 5 years	N=98, M=3.04, SD=0.93	N=127, M=3.13, SD=0.92	0.90 (0.68 to 1.21)	0.92 (0.63 to 1.35)	N=72, M=3.15, SD=1.02	N=126, M=3.08, SD=0.90	1.09 (0.80 to 1.48)	1.30 (0.87 to 1.93)
Child chronic illness	Present	9 (50.0)	9 (50.0)	1.39 (0.53 to 3.66)	2.25 (0.64 to 7.97)	6 (33.3)	12 (66.7)	0.93 (0.33 to 2.61)	0.97 (0.26 to 3.57)
	None	82 (41.8)	114 (58.2)	Reference	Reference	56 (35.0)	104 (65.0)	Reference	Reference
Child up-to-date with other routine vaccines	Not fully UTD	5 (50.0)	5 (50.0)	1.35 (0.38 to 4.81)	1.16 (0.24 to 5.68)	3 (50.0)	3 (50.0)	1.90 (0.37 to 9.70)	1.42 (0.21 to 9.72)
	UTD	86 (42.6)	116 (57.4)	Reference	Reference	59 (34.5)	112 (65.5)	Reference	Reference

*$p \leq .05$

[a] Adjusting for all other personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines)
Abbreviations. UTD = up-to-date

6.2.2 Side-effect reporting

At T2, 98 people out of 227 who completed the question (43.2%, 95% CI [36.7, 49.7]) reported at least one side-effect. At T3, 72 people out of 200 who completed the question (36.0%, 95% CI [29.3, 42.7]) recalled at least one side-effect. Associations between personal characteristics, predictor variables and side-effect report can be found in Table 16, Table 17 and Table 18.

Three days after their child's vaccination, parents were more likely to report side-effects in boys; if they had expected their child to experience side-effects; and if they had perceived a suggestion of side-effects from the media, NHS vaccination leaflet, or healthcare worker during their vaccination appointment. When taking into account trust in the source of information on the suggestion of side-effects, only trust and suggestions from healthcare workers increased the odds of reporting side-effects.

One month after their child's vaccination, parents were more likely to recall that their child had experienced side-effects if they had expected side-effects; perceived a suggestion of side-effects from the NHS vaccination leaflet; had high trait anxiety; high pessimism; and if they perceived their child to be sensitive to medicines. Perceiving oneself not to know enough about the vaccine was also associated with the recall of side-effects one month after the child's vaccination.

Table 17. Psychological predictors and associations with perception of side-effects from vaccination

Category	Psychological predictor	Level	Side-effects reported at T2				Side-effects reported at T3			
			Side-effects perceived n=98, n (%)	No side-effects perceived n=129, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Side-effects perceived n=72, n (%)	No side-effects perceived n=128, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]
Presence of pre-existing symptoms	Symptom in last 24 hrs	Yes	35 (44.3)	44 (55.7)	1.11 (0.63 to 1.93)	1.06 (0.50 to 2.24)	23 (31.1)	51 (68.9)	0.75 (0.41 to 1.39)	0.72 (0.32 to 1.63)
		No	59 (41.8)	82 (58.2)	Reference	Reference	45 (37.5)	75 (62.5)	Reference	Reference
Direct measure of expectation	Expectation for child to get side-effects	5-point Likert (1='very unlikely' to 5='very likely')	N=98, M=3.13, SD=0.83	N=128, M=2.62, SD=0.94	1.89 (1.39 to 2.58)*	2.09 (1.35 to 3.22)*	N=72, M=3.06, SD=0.87	N=127, M=2.65, SD=0.97	1.60 (1.16 to 2.20)*	2.09 (1.33 to 3.31)*
Source of suggestion of symptoms - expectation	Suggestion of side-effects by friends/family/relatives	4-point Likert (1='very unlikely' to 4='very likely')	N=61, M=2.44, SD=0.72	N=83, M2.41, SD=0.75	1.06 (0.68 to 1.67)	1.32 (0.73 to 2.37)	N=47, M=2.43, SD=0.77	N=83, M=2.39, SD=0.75	1.07 (0.67 to 1.73)	1.54 (0.80 to 2.99)
	Suggestion of side-effects by official websites/helplines/departments/agencies	4-point Likert (1='very unlikely' to 4='very likely')	N=65, M=2.09, SD=0.70	N=94, M=2.12, SD=0.75	0.95 (0.62 to 1.48)	1.37 (0.76 to 2.46)	N=44, M=2.18, SD=0.62	N=96, M=2.05, SD=0.75	1.30 (0.78 to 2.16)	1.80 (0.92 to 3.53)
	Suggestion of side-effects by the media	4-point Likert (1='very unlikely' to 4='very likely')	N=49, M=2.51, SD=0.79	N=73, M=2.42, SD=0.87	1.13 (0.73 to 1.75)	1.87 (1.01 to 3.46)*	N=34, M=2.53, SD=0.86	N=72, M=2.38, SD=0.85	1.24 (0.77 to 2.01)	1.64 (0.84 to 3.20)
	Suggestion of side-effects by the NHS vaccination leaflet	4-point Likert (1='very unlikely' to 4='very likely')	N=68, M=2.26, SD=0.75	N=98, M=2.09, SD=0.80	1.33 (0.89 to 1.99)	1.79 (1.02 to 3.15)*	N=45, M=2.33, 0.74	N=100, M=2.04, SD=0.79	1.62 (1.02 to 2.58)*	2.15 (1.14 to 4.05)*
	Suggestion of side-effects by the HCW in the vaccine appointment	4-point Likert (1='very unlikely' to 4='very likely')	N=61, M=2.64, SD=0.71	N=69, M=2.39, SD=0.69	1.68 (1.00 to 2.81)*	2.27 (1.15 to 4.49)*	N=41, M=2.61, SD=0.54	N=69, M=2.42, SD=0.74	1.55 (0.85 to 2.84)	1.70 (0.85 to 3.43)
	Suggestion of side-effects by friends/family/relatives, by trust	by Trust (range 2 to 16)	N=60, M=8.52, SD=3.19	N=80, M=8.20, SD=2.83	1.04 (0.93 to 1.16)	1.13 (0.98 to 1.30)	N=47, M=8.38, SD=3.27	N=81, M=8.42, SD=2.97	1.00 (0.89 to 1.12)	1.08 (0.93 to 1.26)
	Suggestion of side-effects by official websites/helplines/departments/agencies, by trust	by Trust (range 2 to 20)	N=65, M=8.62, SD=3.44	N=91, M=8.79, SD=3.50	0.99 (0.90 to 1.08)	1.02 (0.91 to 1.15)	N=44, M=8.68, SD=3.48	N=93, M=8.87, SD=3.63	0.99 (0.89 to 1.09)	1.02 (0.90 to 1.17)

	Suggestion of side-effects by the media, by trust	by Trust (range 2 to 20)	N=49, M=8.14, SD=3.61	N=70, M=7.56, SD=3.01	1.06 (0.94 to 1.18)	1.13 (0.98 to 1.31)	N=34, M=8.00, SD=3.82	N=69, M=7.83, SD=3.15	1.02 (0.90 to 1.15)	1.05 (0.89 to 1.23)
	Suggestion of side-effects by the NHS vaccination leaflet, by trust	by Trust (range 1 to 20)	N=68, M=9.84, SD=3.83	N=95, M=9.14, SD=3.87	1.05 (0.97 to 1.14)	1.09 (0.98 to 1.22)	N=44, M=10.09, SD=4.02	N=97, M=9.24, SD=3.96	1.06 (0.97 to 1.16)	1.09 (0.97 to 1.23)
	Suggestion of side-effects by the HCW in the vaccine appointment, by trust	by Trust (range 1 to 20)	N=61, M=11.52, SD=3.58	N=69, M=10.19, SD=3.92	1.10 (1.00 to 1.21)*	1.15 (1.02 to 1.30)*	N=41, M=11.29, SD=2.57	N=69, M=10.38, SD=4.24	1.07 (0.96 to 1.19)	1.07 (0.95 to 1.21)
Social observation - expectation	Knowing another child with side-effects	Yes	16 (47.0)	18 (53.0)	1.20 (0.58 to 2.50)	1.55 (0.61 to 3.89)	11 (40.7)	16 (59.3)	1.26 (0.55 to 2.89)	2.04 (0.76 to 5.46)
		No	82 (42.5)	111 (57.5)	Reference	Reference	61 (35.3)	112 (64.7)	Reference	Reference
	Severity of side-effects observed in other children	5-point Likert (1='very mild to 5='very severe')	N=16, M=2.06, SD=0.68	N=18, M=2.06, SD=0.54	1.02 (0.33 to 3.19)	2.24 (0.20 to 25.49)	N=11, M=2.09, SD=0.30	N=16, M=1.94, SD=0.44	3.12 (0.31 to 31.08)	3.34 (0.02 to 525.68)
Previous symptoms following vaccination	[Child] having side-effects from influenza vaccine previously	Yes	9 (37.5)	15 (62.5)	0.78 (0.30 to 2.05)	0.84 (0.22 to 3.23)	8 (36.4)	14 (63.6)	1.40 (0.50 to 3.90)	2.10 (0.54 to 8.13)
		No	27 (43.5)	35 (56.5)	Reference	Reference	18 (29.0)	44 (71.0)	Reference	Reference
	Worry about [child]'s previous side-effects	4-point Likert (1='not at all' to 4='very worried')	N=9, M=1.78, SD=0.67	N=15, M=1.60, SD=0.83	1.37 (0.46 to 4.14)	†	N=8, M=1.88, SD=0.64	N=14, M=1.64, SD=0.93	1.42 (0.49 to 4.16)	†
	Severity of [child]'s previous side-effects	5-point Likert (1='very mild' to 5='very severe')	N=9, M=1.89, SD=0.60	N=15, M=1.33, SD=0.49	6.88 (1.13 to 42.03)*	†	N=8, M=1.75, SD=0.46	N=14, M=1.29, SD=0.47	7.50 (1.04 to 54.12)*	16.70 (0.45 to 626.15)
	[Child] side-effect from other routine vaccines	Yes	49 (50.5)	48 (49.5)	1.90 (1.08 to 3.35)*	2.10 (1.00 to 4.43)	34 (40.5)	50 (59.5)	1.71 (0.92 to 3.19)	1.842 (0.81 to 4.21)
		No	37 (34.9)	69 (65.1)	Reference	Reference	27 (28.4)	68 (71.6)	Reference	Reference
	Worry about side-effect from other routine vaccine	4-point Likert (1='not at all' to 4='very worried')	N=49, M=1.82, SD=0.70	N=48, M=1.75, SD=0.60	1.17 (0.63 to 2.18)	0.92 (0.37 to 2.27)	N=34, M=1.75, SD=0.46	N=50, M=1.64, SD=0.60	2.00 (0.98 to 4.11)	2.75 (0.98 to 7.74)
Psychological traits	Neuroticism	Range 0 to 6	N=91, M=1.54, SD=1.38	N=120, M=1.72, SD=1.69	0.93 (0.78 to 1.10)	0.94 (0.76 to 1.17)	N=62, M=1.69, SD=1.42	N=114, M=1.64, SD=1.65	1.00 (0.82 to 1.22)	1.05 (0.83 to 1.33)

	Positive affect	Range 5 to 22	N=88, M=15.39, SD=3.98	N=119, M=15.32, SD=3.51	1.01 (0.93 to 1.08)	0.95 (0.86 to 1.04)	N=62, M=14.90, SD=4.18	N=113, M=15.51, SD=3.37	0.96 (0.88 to 1.04)	0.93 (0.85 to 1.03)
	Negative affect	Range 5 to 18	N=88, M=7.92, SD=2.78	N=119, M=7.45, SD=2.73	1.06 (0.96 to 1.18)	1.05 (0.93 to 1.19)	N=62, M=7.77, SD=2.44	N=113, M=7.58, SD=2.86	1.03 (0.92 to 1.15)	1.02 (0.89 to 1.17)
	Anxiety	Range 6 to 19	N=91, M=12.47, SD=2.65	N=120, M=12.87, SD=2.63	0.945 (0.851 to 1.048)	0.993 (0.861 to 1.146)	N=62, M=13.08, SD=2.491	N=114, M=12.67, SD=2.523	1.068 (0.944 to 1.209)	1.192 (1.011 to 1.406)*
	Optimism	Range 1 to 12	N=85, M=7.53, SD=1.817	N=115, M=7.26, SD=1.92	1.081 (0.928 to 1.258)	0.942 (0.783 to 1.134)	N=61, M=7.30, SD=1.856	N=111, M=7.40, SD=1.997	0.973 (0.829 to 1.143)	0.843 (0.688 to 1.032)
	Pessimism	Range 0 to 12	N=85, M=4.29, SD=2.11	N=115, M=4.18, SD= 2.13	1.03 (0.90 to 1.17)	1.15 (0.97 to 1.36)	N=61, M=4.51, SD=1.78	N=111, M=3.89, SD=2.21	1.16 (0.99 to 1.35)	1.25 (1.04 to 1.52)*
Beliefs about medicines and other technologies	Perceived sensitivity to medicines at T1	Range 5 to 25	N=98, M=10.48, SD=3.25	N=129, M=9.40, SD=3.40	1.10 (1.02 to 1.20)*	1.07 (0.97 to 1.19)	N=72, M=10.51, SD=2.72	N=128, M=9.30, SD=3.48	1.12 (1.02 to 1.23)*	1.15 (1.03 to 1.29)*
	Modern Health Worries	Range 28 to 126	N=88, M=67.32, SD=22.670	N=118, M=67.53, SD=20.29	1.00 (0.99 to 1.01)	0.99 (0.97 to 1.00)	N=62, M=68.34, M=21.91	N=113, M=66.25, SD=19.39	1.00 (0.99 to 1.02)	1.00 (0.99 to 1.02)
	Beliefs about Medicines Questionnaire-general, harm subscale	Range 4 to 20	N=91, M=8.73, SD=2.54	N=121, M=8.59, SD=2.73	1.02 (0.92 to 1.13)	1.02 (0.89 to 1.16)	N=62, M=8.55, SD=2.56	N=115, M=8.45, SD=2.72	1.01 (0.90 to 1.14)	1.02 (0.88 to 1.17)
	Beliefs about Medicines Questionnaire-general, overuse subscale	Range 5 to 19	N=91, M=10.84, SD=2.39	N=121, M=10.72, SD=2.74	1.02 (0.92 to 1.13)	1.03 (0.91 to 1.18)	N=62, M=10.79, SD=2.59	N=115, M=10.49, SD=2.72	1.04 (0.93 to 1.17)	1.08 (0.94 to 1.24)

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines)

† Adjusted calculations unable to be run due to lack of cases in some groups.

Abbreviations. NHS = National Health Service, HCW = healthcare worker

Table 18. Beliefs and attitudes about influenza and the child vaccine and associations with perception of side-effects from vaccination

Statement	Level	Side-effects reported at T2				Side-effects reported at T3			
		Side-effects perceived n=98, n (%)	No side-effects perceived n=129, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Side-effects perceived n=72, n (%)	No side-effects perceived n=128, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]
The child flu vaccine has not been tested enough for me to feel it is safe	Agree	9 (60.0)	6 (40.0)	2.25 (0.76 to 6.66)	1.19 (0.25 to 5.69)	8 (66.7)	4 (33.3)	4.62 (1.32 to 16.18)*	6.47 (1.08 to 38.59)*
	Disagree	58 (40.0)	87 (60.0)	Reference	Reference	42 (30.2)	97 (69.8)	Reference	Reference
The child flu vaccine can cause unpleasant short-term side-effects	Agree	23 (57.5)	17 (42.5)	2.07 (0.97 to 4.40)	1.55 (0.57 to 4.24)	11 (36.7)	19 (63.3)	1.45 (0.61 to 3.46)	1.35 (0.44 to 4.18)
	Disagree	36 (39.6)	55 (60.4)	Reference	Reference	26 (28.6)	65 (71.4)	Reference	Reference
The child flu vaccine can cause long-term health problems	Agree	1 (50.0)	1 (50.0)	1.33 (0.08 to 21.68)	0.00 (†)	2 (66.7)	1 (33.3)	4.378 (0.39 to 49.43)	†
	Disagree	72 (42.9)	96 (57.1)	Reference	Reference	48 (31.4)	105 (68.6)	Reference	Reference
The child flu vaccine does not suit my religious or cultural beliefs/values	Agree	6 (85.7)	1 (14.3)	8.21 (0.97 to 69.62)	4.81 (0.46 to 49.86)	3 (75.0)	1 (25.0)	6.28 (0.64 to 61.84)	2.04 (0.12 to 36.17)
	Disagree	76 (42.2)	104 (57.8)	Reference	Reference	53 (32.3)	111 (67.7)	Reference	Reference
I don't like [child] having vaccinations in general	Agree	6 (75.0)	2 (25.0)	3.74 (0.74 to 19.03)	2.93 (0.39 to 21.76)	3 (60.0)	2 (40.0)	2.48 (0.40 to 15.29)	4.23 (0.32 to 55.81)
	Disagree	81 (44.5)	101 (55.5)	Reference	Reference	61 (37.7)	101 (62.3)	Reference	Reference
I don't know enough about the child flu vaccine	Agree	24 (49.0)	25 (51.0)	1.18 (0.60 to 2.32)	1.41 (0.56 to 3.61)	20 (50.0)	20 (50.0)	1.83 (0.87 to 3.85)	3.01 (1.03 to 8.80)*
	Disagree	48 (44.9)	59 (55.1)	Reference	Reference	36 (35.3)	66 (64.7)	Reference	Reference
The vaccination campaign is just about making money for the manufacturers	Agree	3 (42.9)	4 (57.1)	0.99 (0.21 to 4.54)	0.28 (0.01 to 5.23)	4 (66.7)	2 (33.3)	4.08 (0.72 to 22.99)	4.94 (0.37 to 66.52)
	Disagree	73 (43.2)	96 (56.8)	Reference	Reference	52 (32.9)	106 (67.1)	Reference	Reference
The flu vaccine would interact with other medications that [child] is currently taking	Agree	0	0	†	†	1 (100.0)	0 (0.0)	†	†
	Disagree	129 (59.2)	89 (40.8)	Reference	Reference	52 (34.4)	99 (65.6)	Reference	Reference
Vaccinating [child] against flu each year will overload his/her immune system	Agree	9 (69.2)	4 (30.8)	3.13 (0.93 to 10.54)	1.38 (0.27 to 7.10)	5 (50.0)	5 (50.0)	1.96 (0.54 to 7.08)	2.36 (0.42 to 13.39)
	Disagree	72 (41.9)	100 (58.1)	Reference	Reference	53 (33.8)	104 (66.2)	Reference	Reference

Vaccinating [child] against flu each year is too much of an ongoing time commitment	Agree	3 (33.3)	6 (66.7)	0.67 (0.16 to 2.76)	1.16 (0.15 to 9.22)	2 (28.6)	5 (71.4)	0.68 (0.13 to 3.61)	1.10 (0.09 to 13.71)
	Disagree	82 (42.7)	110 (57.3)	Reference	Reference	64 (37.0)	109 (63.0)	Reference	Reference
Having the child flu vaccine is an effective way of preventing [child] from catching flu	Agree	81 (43.3)	106 (56.7)	0.87 (0.30 to 2.51)	0.67 (0.17 to 2.61)	63 (37.0)	107 (63.0)	1.96 (0.52 to 7.40)	2.46 (0.48 to 12.53)
	Disagree	7 (46.6)	8 (53.3)	Reference	Reference	3 (23.1)	10 (76.9)	Reference	Reference
If I don't vaccinate [child], then [child] is likely to catch flu	Agree	28 (52.8)	25 (47.2)	1.36 (0.67 to 2.76)	1.20 (0.48 to 3.01)	23 (44.2)	29 (55.8)	1.85 (0.85 to 4.03)	1.86 (0.69 to 5.02)
	Disagree	33 (45.2)	40 (54.8)	Reference	Reference	18 (30.0)	42 (70.0)	Reference	Reference
Flu would be a serious illness for child	Agree	55 (40.4)	81 (59.6)	0.97 (0.45 to 2.08)	0.71 (0.25 to 1.95)	41 (33.9)	80 (66.1)	1.09 (0.434 to 2.735)	0.90 (0.30 to 2.65)
	Disagree	14 (41.2)	20 (58.8)	Reference	Reference	8 (32.0)	17 (68.0)	Reference	Reference
Flu would be a serious illness for self	Agree	42 (41.2)	60 (58.8)	0.96 (0.50 to 1.86)	0.82 (0.35 to 1.94)	32 (36.4)	56 (63.6)	1.407 (0.647 to 3.060)	1.38 (0.54 to 3.53)
	Disagree	24 (42.1)	33 (57.9)	Reference	Reference	12 (27.3)	32 (72.7)	Reference	Reference
Flu would be a serious illness for someone in child's household	Agree	54 (44.3)	68 (55.7)	1.28 (0.64 to 2.55)	1.09 (0.46 to 2.62)	38 (36.2)	67 (63.8)	1.237 (0.547 to 2.802)	1.11 (0.43 to 2.88)
	Disagree	18 (38.3)	29 (61.7)	Reference	Reference	11 (31.4)	24 (68.6)	Reference	Reference
If [child] were to catch flu, how much, if at all, would it impact your daily life?	4-point Likert (1='not at all' to 4='a great extent')	N=91, M=3.41, SD=0.68	N=122, M=3.41, SD=0.59	0.99 (0.64 to 1.53)	0.92 (0.51 to 1.63)	N=162, M=3.34, SD=0.64	N=115, M=3.50, SD=0.60	0.75 (0.46 to 1.24)	0.81 (0.44 to 1.50)

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines)

† Adjusted calculations unable to be run due to lack of cases in some groups

6.2.3 Expectation as a mediator

The results of mediation analyses are shown in Table 19. Mediation models with estimates for paths a, b, c and c' are illustrated in Figure 8.

When controlling for personal and clinical characteristics, the total effect of suggestion of side-effects from the media on side-effects reported three days after vaccination neared significance, indicating that increased suggestion of side-effects was associated with increased likelihood of side-effect perception (b=.59, p=.06). When taking into account the influence of expectation, there was no direct effect of suggestion of side-effects from the media on side-effects reported three days after vaccination (b=.39, p=.23). 39.5% of the effect of media suggestion of side-effects on side-effects reported three days after vaccination was mediated by expectation.

When controlling for personal and clinical characteristics, there was a total effect of suggestion of side-effects from the NHS vaccination leaflet on side-effects reported three days after vaccination, with increased suggestion of side-effects being associated with increased likelihood of side-effect perception (b=.56, p=.05). The direct effect of suggestion of side-effects from the NHS vaccination leaflet on side-effects reported three days after vaccination was not significant (b=.21, p=.52). 64.1% of the effect of NHS vaccination leaflet suggestion of side-effects on side-effects reported three days after vaccination was mediated by expectation.

When controlling for personal and clinical characteristics, there was a total effect of parents' perception of their child's sensitivity to medicines before vaccination on side-effects reported one month after vaccination, with increased sensitivity being associated with increased likelihood of side-effect perception (b=.14, p=.02). The direct effect of parents' perception of their child's sensitivity to medicines before vaccination on side-effects reported one month after vaccination was not significant (b=.10, p=.10). 36.6% of the effect of parents' perception of their child's sensitivity to medicines before vaccination on side-effects reported one month after vaccination was mediated by expectation.

There was no evidence that the suggestion of side-effects from the NHS vaccination leaflet or pessimism on side-effect perception one month after vaccination were mediated by expectation.

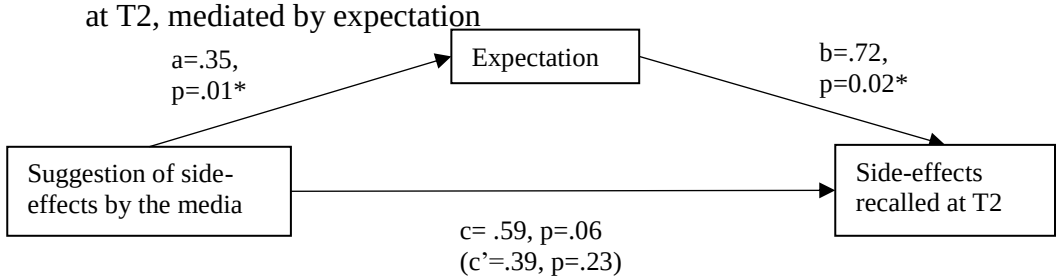
Table 19. Mediation analyses for standardised effects of direct expectation as a mediator for side-effect reporting

Independent Variable	**Mediator**	**Dependent Variable**	**Total indirect effect, β (95% CI)[a]**	**Direct effect, β (95% CI)**	**Total effect, β (95% CI)[a]**	**Proportion of effect mediated**
Suggestion of side-effects by the media	Direct expectation	Side-effects recalled at T2	.10 (.01 to .25)*	.16 (-.20 to .41)	.26 (-.09 to .50)	39.5%
Suggestion of side-effects by the NHS vaccination leaflet	Direct expectation	Side-effects recalled at T2	.14 (.03 to .31)*	.08 (-.22 to .37)	.22 (-.05 to .47)	64.1%
Suggestion of side-effects by the NHS vaccination leaflet	Direct expectation	Side-effects recalled at T3	.10 (-.04 to .27)	.21 (-.11 to .47)	.30 (.03 to .54)*	Not significant
Perceived sensitivity to medicines at T1	Direct expectation	Side-effects recalled at T3	.10 (.02 to .21)*	.17 (-.05 to .38)	.27 (.06 to .46)*	36.6%
Pessimism	Direct expectation	Side-effects recalled at T3	.04 (-.01 to .13)	.21 (-.06 to .41)	.25 (-.02 to .45)	Not significant

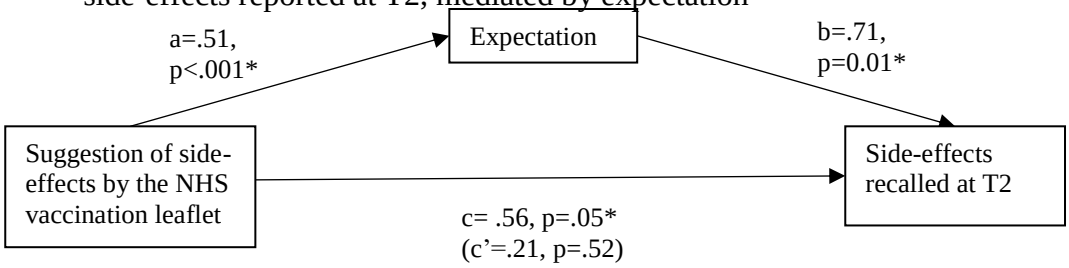
[a] Adjusting for all personal characteristics (both parent and child), apart from child up-to-date vaccine status for other routine vaccines
*$p \leq .05$
Abbreviations. NHS = National Health Service

Figure 8. Mediation models for the unstandardised effects of expectation.

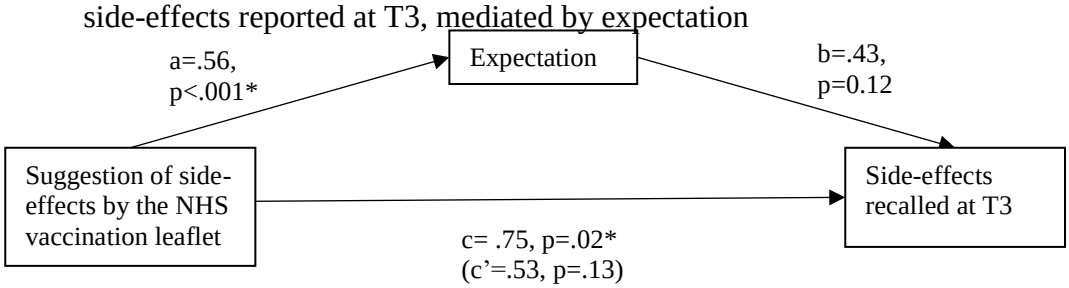
a. Mediation model showing the effect of media suggestion on side-effects reported at T2, mediated by expectation



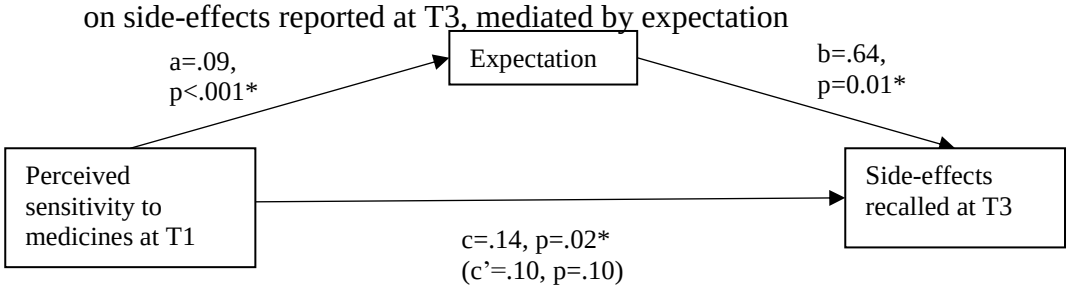
b. Mediation model showing the effect of NHS vaccination leaflet suggestion on side-effects reported at T2, mediated by expectation



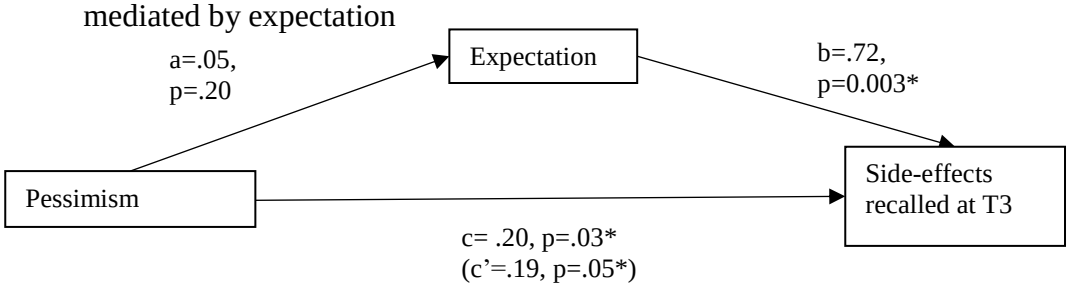
c. Mediation model showing the effect of NHS vaccination leaflet suggestion on side-effects reported at T3, mediated by expectation



d. Mediation model showing the effect of perceived sensitivity to medicines at T1 on side-effects reported at T3, mediated by expectation



e. Mediation model showing the effect of pessimism on side-effects reported at T3, mediated by expectation



*$p \leq .05$
Abbreviations. NHS = National Health Service

6.2.4 Re-vaccination intention for 2017/18

204 (83.6%, 95% CI [78.9, 88.3]) parents indicated that they definitely intended to re-vaccinate their child in the next influenza season (2017/18), while 40 (16.4%, 95% CI [11.7, 21.1]) indicated that they did not definitely intend to re-

vaccinate their child. Associations between personal characteristics, predictor variables and definitely intending to re-vaccinate can be found in Table 20 and Table 21.

Re-vaccination intention was associated with parent age, with parents aged thirty-five to forty-four being more likely to intend to re-vaccinate their child than those aged eighteen to thirty-four.

Decreased re-vaccination intention was associated with higher parental worry about side-effects three days after vaccination; increased perceived severity of side-effects three days after vaccination; parental recall of side-effects one month after vaccination; and higher worry about side-effects one month after vaccination.

6.2.5 Re-vaccination in 2017/18

Vaccination status in 2017/18 was ascertained for 232 participants (response rate 85.9%), of whom 190 were mothers.

Forty-one children (17.7%, 95% CI [12.7, 22.6]) had not been re-vaccinated; 188 children (81.0%, 95% CI [76.0, 86.1]) had been re-vaccinated; and three parents (1.3%) indicated they did not know if their child had been re-vaccinated. Associations between personal characteristics, predictor variables and re-vaccination refusal can be found in Table 20 and Table 21.

Parents who were aged thirty-five to forty-four were less likely to re-vaccinate their child compared to those aged eighteen to thirty-four, however these analyses relied on a cell count of fewer than ten participants and so should be taken with caution. No other personal or clinical characteristics were associated with re-vaccination status.

Parents who reported that their child experienced more severe side-effects three days after vaccination were more likely not to re-vaccinate their child in 2017/18. Parents who reported being more worried about their child's side-effects one month after vaccination were also more likely not to re-vaccinate their child in 2017/18. No other variables showed an association with re-vaccination status.

Table 20. Parent and child personal and clinical characteristics and associations with re-vaccination intention for 2017/18 and re-vaccination status in 2017/18

Participant characteristics	Level	Re-vaccination intention for 2017/18				Re-vaccination in 2017/18 influenza season			
		Do not intend to re-vaccinate n=40, n (%)	Intend to re-vaccinate n=204, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Not re-vaccinated n=41, n (%)	Re-vaccinated n=188, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]
Parent gender	Female	38 (19.0)	162 (81.0)	0.20 (0.05 to 0.88)*	0.40 (0.08 to 2.00)	34 (17.9)	156 (82.1)	1.00 (0.41 to 2.45)	0.50 (0.15 to 1.74)
	Male	2 (4.5)	42 (95.5)	Reference	Reference	7 (17.9)	32 (82.1)	Reference	Reference
Parent age	45+	1 (6.3)	15 (93.8)	4.50 (0.54 to 37.66)	5.28 (0.59 to 47.47)	2 (12.5)	14 (87.5)	0.43 (0.09 to 2.16)	0.46 (0.08 to 2.66)
	35-44	17 (16.5)	86 (83.5)	1.52 (0.66 to 3.48)	2.93 (1.05 to 8.20)*	9 (8.9)	92 (91.1)	0.29 (0.11 to 0.76)*	0.30 (0.09 to 0.96)*
	18-34	12 (23.1)	40 (76.9)	Reference	Reference	12 (25.0)	36 (75.0)	Reference	Reference
Parent chronic illness	Present	7 (14.0)	43 (86.0)	1.37 (0.56 to 3.33)	2.29 (0.56 to 9.33)	6 (13.3)	39 (86.7)	0.83 (0.32 to 2.17)	1.21 (0.33 to 4.41)
	None	30 (18.2)	135 (81.8)	Reference	Reference	24 (15.7)	129 (84.3)	Reference	Reference
Other 'at risk' people in child's household	Yes	14 (17.3)	67 (82.7)	0.73 (0.33 to 1.60)	0.56 (0.22 to 1.62)	9 (12.0)	66 (88.0)	0.74 (0.31 to 1.78)	0.35 (0.10 to 1.20)
	No	15 (13.2)	99 (86.8)	Reference	Reference	16 (15.5)	87. (84.5)	Reference	Reference
Child gender	Female	21 (16.4)	107 (83.6)	0.95 (0.48 to 1.88)	1.71 (0.67 to 4.42)	24 (19.5)	99 (80.5)	1.26 (0.63 to 2.49)	1.66 (0.58 to 4.77)
	Male	18 (15.7)	97 (84.3)	Reference	Reference	17 (16.2)	88 (83.8)	Reference	Reference
First-born child	Yes	23 (17.3)	110 (82.7)	0.97 (0.47 to 2.01)	0.78 (0.28 to 2.16)	19 (15.6)	103 (84.4)	1.09 (0.49 to 2.44)	0.60 (0.20 to 1.86)
	No	14 (16.9)	69 (83.1)	Reference	Reference	11 (14.5)	65 (85.5)	Reference	Reference
Child age	Range 1 to 5 years	N=39, M=3.23, SD=1.04	N=203, M=3.07, SD=0.89	0.83 (0.57 to 1.21)	0.73 (0.43 to 1.22)	N=40, M=3.03, SD=0.92	N=186, M=3.10, SD=0.92	0.91 (0.63 to 1.33)	0.86 (0.48 to 1.55)
Child chronic illness	Present	2 (11.1)	16 (88.9)	1.72 (0.38 to 7.81)	2.39 (0.24 to 23.67)	3 (16.7)	15 (83.3)	1.13 (0.31 to 4.18)	1.92 (0.35 to 10.57)
	None	35 (17.7)	163 (82.3)	Reference	Reference	27 (15.0)	153 (85.0)	Reference	Reference
Child up-to-date with other routine vaccines	Not fully UTD	1 (10.0)	9 (90.0)	0.52 (0.06 to 4.22)	1.42 (0.15 to 13.59)	0 (0.0)	9 (100.0)	†	†
	UTD	36 (17.6)	168 (82.4)	Reference	Reference	29 (15.7)	159 (84.6)	Reference	Reference

*$p \leq .05$
[a] Adjusting for all other personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines)
† Calculations unable to be run due to lack of cases in some groups
Abbreviations: UTD = up-to-date

Table 21. Psychological predictors and associations with re-vaccination intention for 2017/18 and re-vaccination status in 2017/18

Category	Psychological predictor	Level	Re-vaccination intention for 2017/18				Re-vaccination in 2017/18 influenza season			
			Do not intend to re-vaccinate n=40, n (%)	Intend to re-vaccinate n=204, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]	Not re-vaccinated n=41, n (%)	Re-vaccinated n=188, n (%)	Odds ratio (95% CI)	Adjusted odds ratio (95% CI)[a]
Symptoms following vaccination	Presence of side-effects as recalled at T2	Yes	21 (21.4)	77 (78.6)	0.56 (0.28 to 1.12)	0.63 (0.24 to 1.62)	13 (15.7)	70 (84.3)	1.18 (0.54 to 2.62)	2.21 (0.72 to 6.82)
		No	17 (13.2)	112 (86.8)	Reference	Reference	16 (13.6)	102 (86.4)	Reference	Reference
	Worry about side-effects as recalled at T2	4-point Likert (1='not at all' to 4='very worried')	N=21, M=2.19, SD=1.03	N=79, M=1.49, SD=0.58	0.30 (0.15 to 0.59)*	0.26 (0.08 to 0.87)*	N=15, M=1.73, SD=1.03	N=70, M=1.61, SD=0.67	1.24 (0.60 to 2.56)	1.35 (0.44 to 4.18)
	Severity of side-effects as recalled at T2	5-point Likert (1='very mild' to 5='very severe')	N=21, M=2.48, SD=0.87	N=79, M=1.70, SD=0.79	0.35 (0.19 to 0.65)*	0.11 (0.02 to 0.60)*	N=15, M=1.87, SD=1.06	N=70, M=1.79, SD=0.78	1.12 (0.58 to 2.19)	2.83 (1.05 to 7.63)*
	Presence of side-effects as recalled at T3	Yes	16 (22.2)	56 (77.8)	0.40 (0.18 to 0.88)*	0.27 (0.09 to 0.83)*	11 (16.7)	55 (83.3)	0.89 (0.40 to 1.97)	1.45 (0.50 to 4.49)
		No	13 (10.2)	115 (89.8)	Reference	Reference	22 (18.3)	98 (81.7)	Reference	Reference
	Worry about side-effects as recalled at T3	4-point Likert (1='not at all' to 4='very worried')	N=15, M=2.00, SD=0.93	N=55, M=1.55, SD=0.66	0.46 (0.21 to 0.98)*	0.17 (0.03 to 0.92)*	N=11, M=1.82, SD=0.98	N=53, M=1.58, SD=0.66	1.52 (0.65 to 3.56)	4.57 (1.01 to 20.58)*
	Severity of side-effects as recalled at T3	5-point Likert (1='very mild' to 5='very severe')	N=14, M=2.29, SD=0.91	N=52, M=1.75, SD=0.79	0.47 (0.23 to 0.97)*	0.31 (0.08 to 1.14)	N=10, M=2.50, SD=0.71	N=50, M=1.76, SD=0.82	2.83 (1.19 to 6.73)*	8.17 (0.83 to 80.24)
Re-vaccination intention	Re-vaccination intention	Yes	-	-	-	-	31 (17.4)	147 (82.6)	1.31 (0.47 to 3.63)	0.49 (0.13 to 1.90)
		No					5 (13.9)	31 (86.1)	Reference	Reference

Factors which may have changed since vaccination in 2016/17	Suggestion of side-effects by the HCW in the vaccine appointment	4-point Likert (1='very unlikely' to 4='very likely)	N=21, M=2.48, SD=0.87	N=111, M=2.50, SD=0.69	1.06 (0.55 to 2.03)	1.82 (0.67 to 4.95)	N=14, M=2.64, SD=0.63	N=105, M=2.47, SD=0.71	1.47 (0.62 to 3.48)	1.638 (0.52 to 5.18)
	Suggestion of side-effects by the HCW in the vaccine appointment, by trust	by Trust (range 1 to 20)	N=21, M=9.57, SD=5.316	N=111, M=10.97, SD=3.528	1.094 (0.973 to 1.231)	1.297 (1.052 to 1.598)*	N=14, M=10.43, SD=4.80	N=105, M=10.68, SD=3.75	0.98 (0.85 to 1.14)	1.02 (0.83 to 1.25)
	Change in perceived sensitivity to medicines	Range -20 to 8	N=28, M=-0.18, SD=2.75	N=166, M=-0.33, SD=3.45	0.99 (0.87 to 1.12)	1.00 (0.87 to 1.17)	N=32, M=-0.31, SD=3.27	N=148, M=-0.18, SD=3.38	0.99 (0.88 to 1.11)	1.03 (0.89 to 1.20)
	Change in trust in healthcare workers	Range -20 to 10	N=29, M=-1.86, SD=3.64	N=160, M=-0.21, SD=3.69	1.11 (1.01 to 1.22)*	1.07 (0.94 to 1.22)	N=31, M=0.26, SD=3.93	N=146, M=-0.67, SD=3.67	1.08 (0.96 to 1.23)	1.07 (0.89 to 1.27)

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines)

Abbreviations: HCW = healthcare worker

6.2.6 Change in perceived sensitivity to medicines

At T1, the overall mean perceived sensitivity to medicines score was 10.03 (SD=3.34, n=270), while at T3 it was 9.40 (SD=3.36, n=194). There was no difference in parents' perceptions of how sensitive their child was to medicines after their child's influenza vaccination in 2016/17 ($t(193)=1.26$, $p=.21$).

There was no association between reporting side-effects three days after the child's vaccination and change in perceived sensitivity to medicines score (overall model, $R^2=.35$, $F(10,129)=6.30$, $p<.001$). However, an association between side-effect perception one month after the child's vaccination and change in perceived sensitivity to medicines score was found (overall model, $R^2=.39$, $F(10,131)=7.81$, $p<.001$; see Table 22). Parents who recalled that their child experienced side-effects had increased perceptions of their child's sensitivity to medicines compared to those who did not recall side-effects ($\beta=.20$, $p=.01$).

Table 22. Associations between side-effect reporting and parents' perceptions of their child's sensitivity to medicines and trust in healthcare workers

Side-effect reporting	**Level**	**Perceived sensitivity to medicines[a]**			**Trust in healthcare workers[b]**		
		n	***β***	***p***	**n**	***β***	***p***
Side-effects recalled at T2	Side-effects perceived	73	.06	.43	97	-.09	.32
	No side-effects perceived	104	Reference		127	Reference	
Side-effects recalled at T3	Side-effects perceived	71	.20	.01*	72	-.03	.73
	No side-effects perceived	123	Reference		103	Reference	

*$p \leq .05$

[a] Adjusting for all personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines) and perceived sensitivity to medicines at T1

[b] Adjusting for all personal characteristics (both parent and child, apart from child up-to-date vaccine status for other routine vaccines) and trust in healthcare workers at T1

6.2.7 Change in trust in healthcare workers

At T1, the overall mean score on the Meyer Credibility Scale was 21.68 (SD=3.43, n=264), while at T3 it was 21.20 (SD=4.19, n=192). There was no

difference in parents' trust in healthcare workers after their child's influenza vaccination in 2016/17 ($t(188)=1.72$, $p=.09$).

There was no association between change in trust in healthcare workers and reporting side-effects three days (overall model, $R^2=.15$, $F(10,125)=1.98$, $p=.04$), or one month (overall model, $R^2=.138$, $F(10,127)=1.87$, $p=.06$) after the child's vaccination (see Table 22).

6.2.8 Sensitivity analyses

Sensitivity analyses indicated that there were no substantial differences to the results when taking into account the effect of clustering by primary care practice. Only four results were changed: worry about side-effects at T3 was no longer significantly associated with re-vaccination intention; side-effects recalled at T3 were no longer significantly associated with change in parental perceived sensitivity to medicines; perceived severity of side-effects at T2 was no longer significantly associated with re-vaccination in 2017/18; and worry about side-effects at T3 was no longer significantly associated with re-vaccination in 2017/18.

For the mediation analyses, there was no difference to the strength or the significance of any of the main pathway effects. Thus, clustering should not change the results of the binary_mediation analysis macro.

6.2.9 Interpretation bias

6.2.9.1 *Participants*

196 parents initiated the scrambled sentences task of whom 75 fulfilled inclusion criteria. Participant personal and clinical characteristics for those included in interpretation bias analyses and how they differ by side-effect perception, re-vaccination intention and actual re-vaccination are shown in Table 23.

Female parents were more likely to be excluded from the analyses ($\chi^2(1, n=196)=4.28$, $p=.04$). There were no other differences in parent or child personal or clinical characteristics (parent age, parent chronic illness, other 'at risk' people in child's household, child gender, first-born child, child age or child chronic illness) between those who were and were not included in the analyses (see Appendix 15).

Table 23. Parent and child personal and clinical characteristics for those included in interpretation bias analyses and associations with perception of side-effects from vaccination, re-vaccination intention for 2017/18 and re-vaccination status in 2017/18

Participant characteristics		**Side-effects reported at T2**			**Side-effects reported at T3**			**Re-vaccination intention for 2017/18 season**			**Re-vaccination in 2017/18 influenza season**		
	Level	**Side-effects perceived n=29, n (%)**	**No side-effects perceived n=45, n (%)**	**p**	**Side-effects perceived n=17, n (%)**	**No side-effects perceived n=49, n (%)**	**p**	**Do not intend to re-vaccinate n=16, n (%)**	**Intend to re-vaccinate n=59, n (%)**	**p**	**Not re-vaccinated n=11, n (%)**	**Re-vaccinated n=61, n (%)**	**p**
Parent gender	Female	25 (43.9)	32 (56.1)	.16	13 (26.0)	37 (74.0)	1.00	14 (24.1)	44 (75.9)	.34	8 (14.5)	47 (85.5)	.71
	Male	4 (76.5)	13 (23.5)		4 (25.0)	12 (75.0)		2 (11.8)	15 (88.2)		3 (17.6)	14 (82.4)	
Parent age	35+	19 (39.6	29 (60.4)	.93	32 (72.7)	12 (27.3)	.77	11 (22.9)	37 (77.1)	.77	5 (10.4)	43 (89.6)	.16
	18-34	10 (38.5)	16 (61.5)		17 (77.3)	5 (22.7)		5 (18.5)	22 (81.5)		6 (25.0)	18 (75.0)	
Parent chronic illness	Present	6 (31.6)	13 (68.4)	.43	4 (22.2)	14 (77.8)	.76	4 (20.0)	16 (80.0)	1.00	2 (10.5)	17 (89.5)	.72
	None	23 (41.8)	32 (58.2)		13 (27.1)	35 (72.9)		12 (21.8)	43 (78.2)		9 (17.0)	44 (83.0)	
Other 'at risk' people in child's household	Yes	12 (41.4)	17 (58.6)	.88	8 (30.8)	18 (69.2)	.40	7 (24.1)	22 (75.9)	.23	2 (7.1)	26 (92.9)	.17
	No	15 (39.5)	23 (60.5)		7 (21.2)	26 (78.8)		5 (12.8)	34 (87.2)		8 (21.6)	29 (78.4)	
Child gender	Female	14 (35.9)	25 (64.1)	.47	9 (27.3)	24 (72.7)	.84	8 (20.0)	32 (80.0)	.95	6 (16.2)	31 (83.8)	1.00
	Male	15 (44.1)	19 (55.9)		8 (25.0)	24 (75.0)		7 (20.6)	27 (79.4)		5 (14.7)	29 (85.3)	
First-born child	Yes	18 (38.3)	29 (61.7)	.84	7 (15.9)	37 (84.1)	.01*	11 (22.9)	37 (77.1)	.77	10 (21.3)	37 (78.7)	.08
	No	11 (40.7)	16 (59.3)		10 (45.5)	12 (54.5)		5 (18.5)	22 (81.5)		1 (4.0)	24 (96.0)	
Child age	Range 2 to 5 years	N=29, M=3.00, SD=0.964	N=44, M=2.95, SD=0.939	.84	N=17, M=3.18, SD=1.185	N=48, M=2.92, SD=0.871	.42	N=15, M=3.27, SD=1.100	N=59, M=2.88, SD=0.892	.16	N=11, M=2.45, SD=0.522	N=60, M=3.03, SD=0.991	.01*
Child chronic illness	Present	4 (66.7)	2 (33.3)	.20	0 (0.0)	6 (100.0)	.33	1 (16.7)	5 (83.3)	1.00	2 (33.3)	4 (66.7)	.23
	None	25 (36.8)	43 (63.2)		17 (28.3)	43 (71.7)		15 (21.7)	54 (78.3)		9 (13.6)	57 (86.4)	
Child up-to-date with other routine vaccines	Not fully UTD	0 (0.0)	2 (100.0)	.52	1 (50.0)	1 (50.0)	.45	0 (100.0)	2 (100.0)	1.00	0 (0.0)	2 (100.0)	1.00
	UTD	29 (40.3)	43 (59.7)		16 (25.0)	48 (75.0)		16 (21.9)	57 (78.1)		11 (15.7)	59 (84.3)	

* $p \leq .05$

Abbreviations: UTD = up-to-date

6.2.9.2 *Side-effect perception at T2*

Of parents included in interpretation bias analyses, twenty-nine perceived side-effects in their child three days after vaccination, while 45 did not. Mean bias scores are shown in Table 24.

No personal or clinical characteristics differed by side-effect perception three days after the child's influenza vaccination (see Table 23). There was a main effect of source of health threat ($F(1,72)=16.96$, $p<.001$, $\eta_p^2=.19$) on bias with higher negative bias for naturally-occurring health threats (M=0.36, SD=0.25) than man-made health threats (M=0.20, SD=0.24). There was no main effect of side-effect perception ($F(1,72)=0.17$, $p=.68$, $\eta_p^2=.002$), nor was there an interaction effect ($F(1,72)=2.30$, $p=.13$, $\eta_p^2=.03$).

Table 24. Mean negative interpretation bias scores (95% CI) by perception of side-effects from vaccination, re-vaccination intention for 2017/18 and re-vaccination status in 2017/18

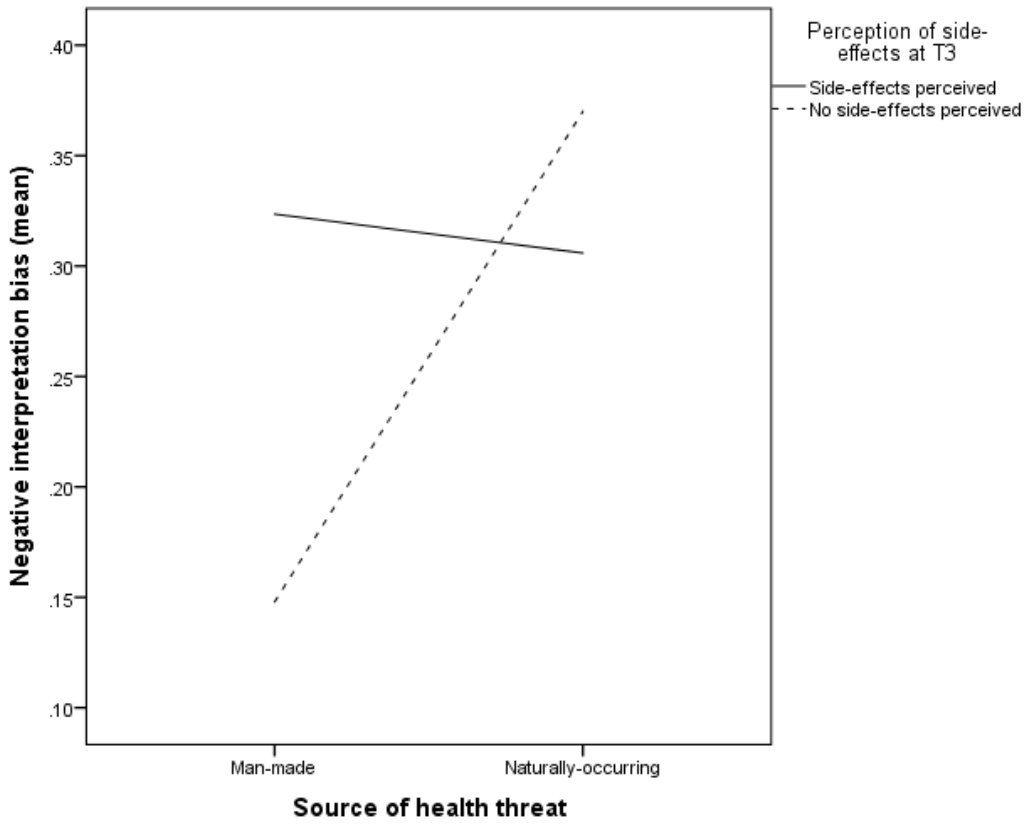
	Side-effects reported at T2		**Side-effects reported at T3**		**Re-vaccination intention for 2017/18 season**		**Re-vaccination in 2017/18 influenza season**	
	Side-effects perceived n=29, mean (95%CI)	**No side-effects perceived n=45, mean (95%CI)**	**Side-effects perceived n=17, mean (95%CI)**	**No side-effects perceived n=49, mean (95%CI)**	**Do not intend to re-vaccinate n=16, mean (95%CI)**	**Intend to re-vaccinate n=59, mean (95%CI)**	**Not re-vaccinated n=11, mean (95%CI)**	**Re-vaccinated n=61, mean (95%CI)**
Man-made health threat	0.25 (0.15 to 0.34)	0.17 (0.10 to 0.24)	0.32 (0.18 to 0.47)	0.15 (0.09 to 0.21)	0.26 (0.13 to 0.38)	0.19 (0.12 to 0.25)	0.24 (0.09 to 0.38)	0.120 (0.14 to 0.26)
Naturally-occurring health threat	0.34 (0.25 to 0.43)	0.38 (0.30 to 0.46)	0.31 (0.16 to 0.45)	0.37 (0.31 to 0.44)	0.37 (0.21 to 0.53)	0.36 (0.30 to 0.43)	0.44 (0.31 to 0.57)	0.34 (0.27 to 0.40)

6.2.9.3 *Side-effect perception at T3*

Of parents included in interpretation bias analyses, seventeen parents perceived side-effects in their child one month after vaccination, while 49 did not. Mean bias scores are shown in Table 24.

There was a group difference between those who did and did not perceive side-effects one month after vaccination for first-child status (χ^2(1, n=66)=6.67, *p*=.01, see Table 23). Therefore, first-child status was entered into the regression model as the first block. Negative bias was associated with perception of side-effects one month after vaccination (aOR=20.59, 95% CI [1.76 to 236.09]). There was a significant interaction effect between negative bias and source of health threat (aOR=0.02, 95% CI [0.001 to 0.66]; see Figure 9). Within group contrasts indicated that there was a significant difference in bias for man-made and naturally-occurring health threats in those who did not perceive side-effects (mean difference=-.22, 95% CI [-.30 to -.15], t(48)=-5.91, *p*<.001, *d*=-1.01), but no difference in those who did perceive side-effects (mean difference=.02, 95% CI [-.17 to .20], t(16)=.21, *p*=.84, *d*=0.06). There was no association between source of health threat and perception of side-effects one month after vaccination (aOR=2.58, 95% CI [0.70 to 9.53]).

Figure 9. Mean negative interpretation bias scores by perception of side-effects at T3



6.2.9.4 *Re-vaccination intention for 2017/18*

Of parents included in interpretation bias analyses, 59 indicated that they definitely intended to re-vaccinate their child, while sixteen did not definitely intend to re-vaccinate. Mean bias scores are shown in Table 24.

No personal or clinical characteristics differed by re-vaccination intention (see Table 23). There was a main effect of source of health threat ($F(1,73)=11.11$, $p<.001$, $\eta_p^2=.13$) on bias with higher negative bias for naturally-occurring health threats (M=0.37, SD=0.25) than man-made health threats (M=0.20, SD=0.24). There was no main effect of re-vaccination intention ($F(1,73)=0.46$, $p=.50$, $\eta_p^2=.01$), nor was there an interaction effect ($F(1,73)=0.63$, $p=.43$, $\eta_p^2=.01$).

6.2.9.5 *Re-vaccination in 2017/18*

Of parents included in interpretation bias analyses, 61 re-vaccinated their child in the 2017/18 influenza season while eleven did not. Mean bias scores are shown in Table 24.

Group differences were found for child age and re-vaccination ($t(-25.66)=-2.85$, $p=.01$, see Table 23). Therefore, child age was entered into the regression model as the first block. There was no association between re-vaccination in 2017/18 and negative bias (aOR=0.47, 95% CI [0.03 to 6.70]) or source of health threat (aOR=2.03, 95% CI [0.35 to 11.75]), nor was there an interaction effect (aOR=0.23, 95% CI [0.004 to 14.28]).

6.3 Discussion

Concern about side-effects is a frequently cited reason for declining vaccination (91, 95, 270). This is a potential problem for the child influenza vaccine as side-effects are common and yearly vaccination is recommended. However, factors affecting parental perception of symptoms have been poorly researched (Chapter 3). The primary aim of this study was to investigate psychological factors associated with parental perception of side-effects.

Pre-vaccination expectations were strongly associated with side-effect reporting both three days and one month after vaccination, indicating the stability of expectations as a predictive factor over time. These results confirm previous findings from cross-sectional research in which parents who thought that their

child would experience a reaction that would need medical treatment from their latest vaccination were more likely to have ever reported their child's side-effects to a health professional or surveillance system (441). Results are also in line with a substantial body of work suggesting that expectations make symptom perception in oneself more likely (220), at least partly because of the increased monitoring for symptoms that can occur as a result of increased expectation. To my knowledge, this is the first time the role of expectation has been demonstrated for the perception of symptoms in someone other than oneself, presumably as a result of a similar monitoring-related mechanism.

Parents who thought that the NHS vaccination leaflet, healthcare worker or the media had suggested that the vaccine caused side-effects were also more likely to report side-effects three days after vaccination. Although I had expected parental trust in a source of information to strengthen the relationship between suggestion of side-effects and later perception of side-effects, when taking into account parental trust, only suggestion from the healthcare worker was associated with side-effect perception. Results indicate that parents' immediate perception of side-effects may be influenced by the number and nature of suggestions of side-effects received, in line with the availability heuristic (442). Only suggestion of side-effects from the NHS vaccination leaflet was associated with side-effect reporting one month after vaccination, implying that while suggestions are important for immediate perception of symptoms, they may be less important in the longer-term recall of those symptoms. The effect of suggestion from the media and the NHS vaccination leaflet were both mediated by direct expectation, indicating that suggestion of side-effects from these sources increases expectations about the incidence of side-effects.

Interestingly, although learning and social observation are associated with the nocebo response (220), I found no effect of having seen other children experience side-effects from the vaccine or having previously perceived side-effects from vaccination in one's own child, on reporting of side-effects. However, analyses investigating previous perception of side-effects from the child influenza vaccine in one's child were underpowered due to small cell counts. Therefore, I may have failed to detect small, but important effects. Another possible explanation for this pattern of results may be that symptom perception is not happening in oneself, as

in previous research, but in one's child. In these situations, parents are unable to access bodily cues and sensations and must attend to and interpret their child's behaviour (443). It is possible that social observation specifically affects bodily sensations.

I also found a gender difference in perception of side-effects, with parents being more likely to report side-effects in boys than girls three days after vaccination. The reasons for this are unclear. Contrary to my results, another study has found that a higher proportion of mothers contacted healthcare workers about side-effects experienced by their female, rather than male child, three days after their child's diphtheria, pertussis and tetanus vaccination (444). However, these results may not be directly comparable, as they relate to parental behaviour in response to side-effects, rather than perception of side-effects per se (445).

Exclusively associated with recall of side-effects one month after vaccination was the feeling that one did not know enough about the vaccine, as well as personality traits such as anxiety and pessimism. The effect of beliefs and personality traits should be treated with caution as confidence intervals for the effect of the former were wide, and the effect sizes of the latter were small. However, these results suggest that different factors are more influential for the medium-term recall of side-effects compared to the immediate perception of side-effects, and are consistent with findings that general negative affect is associated with negative memory bias (446).

The perception that one's child is particularly sensitive to medicines was also associated with recall of side-effects one month after vaccination. This effect was mediated by parents' expectations of how likely their child was to experience side-effects from the vaccine. Again, this is consistent with evidence suggesting that such perceptions can prompt people to monitor for evidence that is in line with their expectations (275). I also found evidence that a feedback loop might be in operation – parents who recalled symptoms one month after vaccination also tended to have elevated perceptions of their child's sensitivity to medicines. However, these results should be taken with caution as there was no longer an association when taking into account clustering by primary care practice. Whether this effect persists in the long term is unknown.

As might be expected in a cohort of parents who have already vaccinated their child once (270), most of my participants intended to vaccinate their child again the following year. However, one in six parents were less than certain in their intentions. Factors that strongly predicted being uncertain about re-vaccination intention were perceived severity and worry about side-effects three days after vaccination and recalling one month later that the child had experienced side-effects. However, worry about side-effects was no longer associated with re-vaccination intention when taking into account the effect of clustering by primary care practice. These results are in line with evidence indicating that fear of side-effects is associated with vaccine hesitancy (447).

This was the first study to investigate re-vaccination rates for the child influenza vaccine in England, with results indicating that 18% of children who were vaccinated in the 2016/17 influenza season were not re-vaccinated in the 2017/18 season. Although previous vaccination has been repeatedly suggested as one of the strongest predictors of future vaccine uptake (93, 130, 408), my study suggests that we cannot rely on this trend to maintain vaccination rates over time, with over one in six children who initially received the influenza vaccine being lost to the vaccination programme in the subsequent year. This disappointingly high proportion of children not re-vaccinated for influenza highlights the need to identify factors associated with re-vaccination refusal and to incorporate these into communications with parents whose children have just been vaccinated.

While parental perception of side-effects was not associated with re-vaccination, parental worry about, and perceived severity of, side-effects were associated with not re-vaccinating one's child. This is in line with the wealth of evidence indicating that parents do not vaccinate their child for fear of side-effects (91, 95, 270) and highlights the importance of parental perception of side-effects in the child influenza vaccination decision. Worry about, and perceived severity of side-effects may impact vaccine uptake through the omission bias, with parents judging the potential adverse effects of vaccinating as worse than adverse effects associated with the child contracting influenza (183). However, these findings should be taken with caution as there was no longer an association when taking into account clustering by primary care practice.

Interestingly, my data also suggest that re-vaccination intention was not associated with later re-vaccination. However, caution should be taken when interpreting this result as analyses may have been underpowered due small cell counts for those who did not intend to re-vaccinate their child. While this may be a manifestation of the intention-behaviour gap commonly found in studies of health behaviours (417), this pattern of results is different to other research which has found parental intention to be associated with later vaccine uptake (113, 448). One factor which might have reduced the importance of intention in this study is the year-long delay between completion of the two measures. It is possible that novel information about the vaccine may have changed parents' re-vaccination intention and subsequent behaviour in this time. Practical considerations, such as the child being ill on the day of vaccination, or vaccine shortages (179) may also be particularly influential in child influenza vaccination, limiting the potential impact of psychological factors.

In relation to my interpretation bias analyses, I found evidence that people consistently interpret health threats from naturally-occurring sources (e.g. bacteria and germs) more negatively than health threats from man-made sources (e.g. medications and mobile phones). This is in line with results from my cross-sectional study (Chapter 5), with findings reflecting the relatively benign nature of the man-made health threats included in study materials.

Parental interpretation biases were associated with perceiving side-effects from the child influenza vaccine, with evidence for a significant interaction effect between bias and perception of side-effects at T3. Parents who perceived side-effects from vaccination made similarly negative interpretations of man-made and naturally-occurring health threats. However, those who did not perceive side-effects had more positive interpretations of man-made health threats than naturally-occurring health threats. These results suggest that increasingly negative interpretations of man-made health threats may influence parental perception of side-effects. This is mirrored in the wider literature, with evidence indicating that worry about modern, man-made health threats is associated with increased symptom perception in oneself (278-281) and the belief that one's child's health was affected by an environmental exposure (248). Similarly, another study also found that those who had a negative interpretation of the word 'vaccination,'

associating it with needles and syringes, were more likely to have ever perceived side-effects from vaccination (287). Though no associations were found between side-effect perception and interpretation biases in the cross-sectional study (Chapter 5), the results from this prospective cohort study are consistent with the notion that parental interpretation biases play a causal role in parental perception of vaccine side-effects.

Interpretation bias may influence perception of side-effects through worry. Interpretation bias is thought to play a causal and maintaining role in worry (449), and associations between interpretation bias and worry and rumination have been found in healthy individuals (450), as well as those with generalised anxiety disorder (451, 452) and depression (452). Interpretation biases about man-made and naturally-occurring health threats may underlie worry about adverse effects and worry about the severity of the illness, respectively. Worry is associated with increased symptom perception in everyday life (247, 248, 278-281). In this case, interpretation bias may have caused worry about vaccine side-effects, which in turn affected parental perception of side-effects from vaccination.

I found no evidence for an association between parental interpretation biases and intended or actual re-vaccination behaviour. This is a difference to findings from my cross-sectional study, in which biases were associated with vaccine uptake and vaccination intention (Chapter 5). Cognitive biases have also been associated with the uptake of other public health behaviours, such as alcohol consumption (203, 204), smoking behaviour (205, 453, 454) and healthy eating (206, 455). Multiple differences between these studies and my study could explain why I did not find an association. First, studies into smoking cessation and unhealthy eating relate to habitual behaviours completed every day; parents must make the decision to vaccinate their child for influenza once a year. Second, studies investigating smoking and healthy eating looked at associations with attention bias, while I investigated interpretation bias. Third, parental interpretation biases were measured one year before child re-vaccination. Other external pressures could have come into play in this time, such as having encountered novel negative information about the child influenza vaccine. Side-effect perception may be less influenced by external pressures and circumstantial factors than re-vaccination, explaining why an association between interpretation bias and side-

effect perception was found. Fourth, circumstantial factors may have influenced re-vaccination, such as lack of the vaccine at the child's general practice (179), the influence of one's partner in the vaccination decision and other practicalities associated with taking the child to be vaccinated (see Chapter 2). Fifth, although power analyses indicated that I was well powered to detect medium effect sizes, there was an imbalance in numbers between those who did and did not re-vaccinate their child (n=61 and n=11 respectively). It is also possible that parental interpretation bias exerted a small effect on re-vaccination behaviour, which I was unable to detect.

6.3.1 Limitations

Several limitations should be considered for this study. First, my sample may not be fully representative of the wider population of vaccinating parents. However, rates of side-effect perception identified in this study (43.2%) are close to those found in clinical trial data (47.9%) (77) and in the demographically representative survey presented in Chapter 5 (41.0%), suggesting that no major systematic bias exists with regards to my main outcome.

Second, my sample was mostly made up of mothers and I cannot say whether these findings would hold in a population of fathers.

Third, interpretation bias analyses were run on a subsection of the overall sample: those who completed the scrambled sentence task to levels which satisfied inclusion criteria. Female parents were more likely to be excluded from the analyses than male parents. Interpretation biases of parents completing the study, and those included in analyses, may not have been representative of interpretation biases held by the wider population.

Fourth, not all potential predictors were measured at T1 due to time constraints as parents completed materials before their child's vaccination appointment. However, only variables which should not change between time points, such as demographics and personality traits, were measured at T2.

Fifth, it is possible that a child may have been vaccinated privately even if their vaccination record from the primary care clinic indicated that they had not been vaccinated in the 2017/18 influenza season. This seems unlikely, given that the

vaccination was available without cost through the primary care practice and at school. Nonetheless, to combat this risk, parents of all children who were eligible to receive the vaccine at school were contacted to ascertain their child's vaccine status.

Sixth, the study was powered to find medium effect sizes in ANOVA and logistic regression analyses, but it is possible that I failed to detect small size effects. In particular, interpretation bias analyses were underpowered. Few parents indicated that they did not definitely intend to re-vaccinate their child in 2017/18, or that they did not re-vaccinate their child in 2017/18, leading to an imbalance in group numbers and a resulting lack of power. Thus, the interpretation of some results should be taken with caution due to resulting wide confidence intervals.

Finally, results should be interpreted with caution due to the large number of analyses run, which increases the likelihood of type 1 errors.

6.3.2 Conclusions

This study suggests that to decrease side-effect perception and recall, parental expectations of side-effects following vaccination should be minimised. By managing parents' expectations about the incidence and severity of side-effects and by decreasing parental concern about side-effects, more parents may decide to re-vaccinate their child. There is some evidence that a tendency to interpret man-made health threats more negatively may also underlie parental perception of side-effects from vaccination. My results indicate that over one in six children were not re-vaccinated for influenza in the 2017/18 season, despite being vaccinated in 2016/17. While there was no evidence for a role of other psychological factors in child influenza re-vaccination, perhaps due to the year-long gap between measurements, the effect of parental perception of severe side-effects from vaccination and worry about side-effects persisted, negatively influencing re-vaccination. These results highlight the need to focus on minimising parental perception of, and worry about, vaccination side-effects to maintain vaccine uptake rates.

Chapter 7. General discussion

Since its introduction to the UK vaccine schedule, low uptake of the child influenza vaccine means that the burden of influenza on healthcare services is still considerable. During the 2017/18 influenza season, 2.8% of all general practice consultations and 1.3% of all calls to NHS 111 in England were attributed to cold or influenza (59). In the UK, there were 372 deaths from laboratory-confirmed influenza in 2017/18, of which sixteen were children (59). Influenza vaccine history was available for six of these children; none had been vaccinated that year (59). The 2018/19 season has brought further initiatives to increase child influenza vaccine uptake. Parents of one child for whom influenza was fatal have started the social media campaign #ThumbsUpForCoby, which is supported by the Devon NHS Clinical Commissioning Group (456). Whether efforts are successful in increasing uptake remains to be seen.

My thesis aimed to identify psychological factors associated with child influenza vaccination in England and with parental perception of side-effects from the vaccine. I was also interested in how the perception of side-effects and other psychological factors influenced re-vaccination rates in those vaccinated for influenza the previous year. In this chapter, I will summarise my hypotheses and whether they are supported, what we have learned and discuss my findings in the context of the wider literature. I will then consider the practical implications my findings have for public health and future research.

7.1 Overview of hypotheses and empirical support

In Chapter 4, I outlined a number of hypotheses for factors associated with child influenza vaccine uptake, re-vaccination, and parental perception of side-effects. Table 25 summarises these hypotheses and outlines whether hypotheses were supported by studies in the thesis.

Table 25. Summary of and support for hypotheses

Outcome	Section	Factor hypothesised to be related to outcome (relates to parent unless otherwise stated)	Supported
Vaccine uptake (refusing vaccination, not intending to vaccinate)	4.1.1	Believe influenza was benign	Supported
	4.1.2	Have negative beliefs and attitudes about vaccinations in general and the child influenza vaccine in particular	Supported
	4.1.3	Interpretation bias. a. Source of health threat b. Subject of health threat	a. Supported b. Not supported
	4.1.4	No history of previous child influenza vaccination (child)	Supported
Re-vaccination (negative re-vaccination intention, re-vaccination refusal)	4.2.1	Perceived side-effects from vaccination	T2 not supported. T3 partially supported.
	4.2.2	Perceived more severe side-effects	T2 partially supported. T3 not supported.
	4.2.3	Higher worry about side-effects perceived	T2 partially supported. T3 partially supported.
	4.2.4	Heard from healthcare worker in the vaccination appointment that the vaccine caused side-effects	Not supported
	4.2.5	Thought the child was more sensitive to medicines after they had been vaccinated for influenza	Not supported
	4.2.6	Had less trust in the healthcare worker after their child had been vaccinated for influenza	Not supported
	4.2.7	Interpretation bias. a. Source of health threat b. Subject of health threat	a. Not supported b. Not tested
	4.2.8	Parents who did not intend to re-vaccinate their child would be less likely to re-vaccinate their child	Not supported
Parental perception of side-effects	4.3.1	Report symptoms in the child before vaccination	Not supported
	4.3.2	Expect their child to develop side-effects from vaccination	Supported
	4.3.3	Have negative beliefs about medicines	Not supported
	4.3.4	Think their child was more sensitive to medicines	T3 not supported. T3 supported.
	4.3.5	Have increased modern health worries	Not supported
	4.3.6	Believe influenza was benign	Not supported
	4.3.7	Have negative beliefs and attitudes about vaccinations in general and the child influenza vaccine in particular	Not supported
	4.3.8	Have increased trait anxiety	T2 not supported. T3 supported.
	4.3.9	Have increased negative affect	Not supported
	4.3.10	Have increased neuroticism	Not supported
	4.3.11	Have increased pessimism	T2 not supported. T3 supported.
	4.3.12	Have decreased positive affect	Not supported
	4.3.13	Have decreased optimism	Not supported

4.3.14	Interpretation bias. a. Source of health threat b. Subject of health threat	a. Partially supported b. Not supported
4.3.15	Parental expectations might mediate the relationship between psychological predictors and parental perception of side-effects	T2 supported. T3 partially supported.

7.2 Factors associated with child influenza vaccine uptake

Factors associated with vaccine uptake have been well-researched (91, 93, 95, 182, 270). However, my study was the first to investigate psychological factors associated with uptake of the child influenza vaccine since its introduction to the vaccine schedule in England. I investigated factors associated with vaccine uptake in the 2015/16 influenza season using a cross-sectional study. In my study 52.8% of children were vaccinated (Chapter 5); similar to official national uptake rates for that year (57).

Many theories of behaviour such as the health belief model, the theory of planned behaviour, the protection motivation theory and the health action process approach postulate that attitudes about perceived risks and benefits play a key role in uptake of health behaviours (87-89, 418). In line with my hypotheses (Hypothesis 4.1.1, Hypothesis 4.1.2), I found good evidence for a role of parental beliefs and attitudes in child influenza vaccination. In line with results from my systematic review of vaccine uptake (Chapter 2), I found that acceptance of the child influenza vaccine in 2015/16 was associated with believing that the vaccine was effective, that vaccination had been recommended by a health professional and that influenza was a serious illness in my cross-sectional study (Chapter 5). Vaccine refusal was associated with the belief that the vaccine could cause adverse effects, that the vaccination campaign was about making money for the manufacturers, and uncertainty-related beliefs such as feeling that you did not know enough about the vaccine (Chapter 5). Other surveys investigating beliefs about vaccine safety and efficacy, attitudes about vaccine mandates and exemptions, trust, mistrust of vaccine benefit, worries about unforeseen future effects, concerns about commercial profiteering, and preference for natural immunity (419, 457) have also found associations with child vaccination (135, 419). My results are also in keeping with findings from other studies investigating

parental attitudes and child influenza vaccine uptake in the UK that have been published since I conducted the cross-sectional study (420, 421).

My cross-sectional study was also the first to investigate the relationship between parental interpretation biases and child vaccination (Hypothesis 4.1.3). Parents who vaccinated their child in the 2015/16 influenza season tended to interpret naturally-occurring health threats more negatively and man-made health threats less negatively than those who did not vaccinate their child; this pattern was also seen for those who intended to vaccinate their child in 2016/17 (Chapter 5). These results are the first to indicate that there is an association between parental interpretation biases and vaccination behaviour, in line with research indicating that information processing biases are associated with the uptake of other public health behaviours (203-206, 208). Interpretation biases mirror factors consistently associated with vaccination refusal, namely the perception that the vaccine causes adverse effects and the benign appraisal of the illness (Chapter 2). Biases in threat appraisal may therefore exist at the information processing level, acting as an underlying mechanism influencing child vaccination.

I also investigated parental interpretation biases pertaining to the subject of the health threat (self- or child-relevant) in relation to vaccine uptake, finding no evidence for an association (Hypothesis 4.1.3). Although there was a slight tendency for parents who had vaccinated their child for influenza in 2015/16 and who intended to vaccinate their child in 2016/17 to interpret threats to their child's health more negatively than those who did not, this difference was not statistically significant. My study was the first to investigate the association between parental interpretation biases for health threats in the child's environment and uptake of a health behaviour. Previous research aimed to investigate whether parents showed biased interpretation in ambiguous situations involving their child, rather than themselves (198-200).

There was good evidence for my hypothesis that previous influenza vaccination would be associated with child influenza vaccine uptake in 2015/16 (Hypothesis 4.1.4, Chapter 5). Previous vaccination has been identified as a strong predictor of current vaccination in the literature (93, 182, 270).

I also used the cross-sectional study to explore whether parent or child personal or clinical characteristics were associated with child influenza vaccine uptake in 2015/16. I found no evidence for associations between vaccine uptake and parent or child personal or clinical characteristics. Since having conducted the cross-sectional study, another study has investigated personal characteristics associated with child influenza vaccine uptake in England and Wales (458). This study investigated factors associated with vaccine uptake in the 2014/15 season, finding that children were more likely to be vaccinated if they were: aged two compared to those aged four; and in a clinical risk group compared to those not in a clinical risk group. This study had a larger sample size than mine (n=57,545) and would have had greater power to detect small effects than I did.

7.3 Factors associated with re-vaccination in those who had already received the child influenza vaccine

My prospective cohort study sample was made up of parents who had already chosen to vaccinate their child for influenza in the 2016/17 influenza season; as such I was unable to investigate vaccine uptake rates. Instead, I used this study to investigate rates of intended re-vaccination for 2017/18 and actual re-vaccination in 2017/18. In this sample, 16.4% of parents indicated that they did not definitely intend to re-vaccinate their child in 2017/18, with 17.7% actually not re-vaccinating their child. These are the first estimates of re-vaccination rates for the child influenza vaccine in England. This is surprising in itself. While a focus on getting parents to engage with the vaccination programme in the first place is clearly important, understanding why some subsequently fail to re-vaccinate their child as requested is also important. My finding that over one in six children are not re-vaccinated makes this especially true.

Despite the central role that intention plays in many theories of behaviour (88, 89, 418), I found no evidence that re-vaccination intention for 2017/18 was associated with re-vaccination in 2017/18 (Hypothesis 4.2.8, Chapter 6). One possible explanation for this is that few participants who indicated that they did not definitely intend to re-vaccinate their child also indicated that they had not re-vaccinated their child, leading to a small cell count. Consequently, this analysis lacked power, meaning that I was unable to detect anything other than relatively

large effects. While this remains the most likely reason for not finding an association between re-vaccination intention and re-vaccination behaviour, other factors may also have played a role. For example, practical considerations, such as the child being ill on the day of vaccination, or vaccine shortages (179) may have been influential in child influenza re-vaccination, limiting the potential impact of psychological factors. In my study, there was a tendency for children originally vaccinated at their general practice surgery in 2016/17 to be re-vaccinated at school in 2017/18. This was partly as a result of children reaching school age between the two time points and partly because of changes to official recommendations in the 2017/18 influenza season, stating that children aged four be vaccinated at school rather than at their primary care practice (55, 459). This may also have reduced the impact of intention in my study.

The perceived risk of potential adverse effects from vaccination is one of the factors most consistently associated with vaccination refusal (91, 93, 95, 270). But do parents still decide to have their child vaccinated for influenza after having perceived side-effects from previous influenza vaccinations (Hypothesis 4.2.1)? I found evidence that having perceived side-effects from the influenza vaccine lowers parents' intentions to re-vaccinate their child in the following season, but does not affect actual re-vaccination rates. In my cross-sectional study, parents who had vaccinated their child in the 2015/16 influenza season were asked whether they had perceived side-effects from vaccination or not. Those who had perceived side-effects showed decreased re-vaccination intention for the 2016/17 season compared to those who had not perceived side-effects (Chapter 5). Longitudinal evidence from my prospective cohort study indicated that reporting side-effects one month, but not three days, after vaccination in 2016/17 was associated with not definitely intending to re-vaccinate in 2017/18 (Chapter 6). I found no evidence for an association between parental perception of side-effects either three days or one month after vaccination and actual re-vaccination in 2017/18 (Chapter 6).

While side-effect perception alone may not have impacted re-vaccination behaviour, I found evidence that emotion-related variables such as worry about side-effects and perceived severity of side-effects were associated with not intending to re-vaccinate and re-vaccination refusal (Hypothesis 4.2.2,

Hypothesis 4.2.3, Chapter 5, Chapter 6). Perceived severity of side-effects may impact vaccine uptake through worry, with those who perceive more severe side-effects being more worried about them. My findings are in line with research indicating that vaccine uptake may be more strongly associated with emotion-related variables, such as perceived responsibility and anticipated regret, than variables which are associated with beliefs about the probability of benefits and risks of vaccination (460, 461). However, results should be taken with caution as perceived severity of side-effects three days after vaccination, and worry about side-effects one month after vaccination were no longer significantly associated with re-vaccination in 2017/18 when taking into account the effect of clustering by primary care practice.

I hypothesised that a suggestion from the healthcare worker in the vaccination appointment that the vaccine caused side-effects would be associated with reduced intention to re-vaccinate and re-vaccination refusal (Hypothesis 4.2.4). I found no evidence to support this hypothesis. Contrary to my hypothesis, I found that when taking into account parental trust in the healthcare worker, suggestion of side-effects was associated with increased re-vaccination intention for 2017/18 (Chapter 6). One speculative explanation for this is that parents who trusted healthcare workers may have felt more fully informed about the potential adverse effects of vaccination and were therefore more inclined to intend to re-vaccinate their child.

As perceived sensitivity to medicines and trust in healthcare workers have been associated with medication adherence (430, 431), I investigated whether changes in parents' perceptions of their child's sensitivity to medicines and trust in healthcare workers following vaccination in the 2016/17 season were associated with re-vaccination in 2017/18 (Hypothesis 4.2.5, Hypothesis 4.2.6). I found no evidence for either of these hypotheses. One important difference between medication adherence studies and my prospective cohort study may explain this. Medication adherence is usually investigated in populations which take a certain medication daily for a chronic condition, for example diabetes, whereas child influenza vaccination is a single behaviour completed once a year. Perceived sensitivity to medicines and trust in healthcare workers may affect habitual medication uptake more strongly than one-off vaccination behaviours.

In contrast to my finding that vaccination was associated with parental interpretation biases pertaining to the source of the health threat in the cross-sectional study (Chapter 5), I found no evidence that interpretation bias was associated with intended or actual re-vaccination in my prospective cohort study (Hypothesis 4.2.7, Chapter 6). Multiple reasons might explain this finding. First, the year-long gap between measuring interpretation bias and re-vaccination might mean that parental interpretation biases and resulting behaviour had changed in this time. Second, practical aspects affecting re-vaccination behaviour may have masked the effect of interpretation biases on re-vaccination. Third, my prospective cohort study had a restricted sample compared to my cross-sectional study, being made up of parents who had already vaccinated their child in the 2016/17 influenza season. Fourth, parental interpretation biases only exerted a small effect on vaccination in my cross-sectional study (Chapter 5). My cohort study had weaker power to detect effects than my cross-sectional study (Chapter 5, Chapter 6). Thus, it is possible that I failed to detect small effects exerted by parental interpretation biases on re-vaccination in my prospective cohort study.

I did not investigate interpretation biases pertaining to the subject of the health threat (self- or child-relevant) in my prospective cohort study. This was due to the smaller number of participants included in the study compared to the cross-sectional study. Investigating the influence of biases pertaining to both the source and subject of the health threat would have resulted in fewer participants in each group and further decreased power to detect associations. The lack of evidence for associations between bias pertaining to the source of the health threat and any outcome measure in my cross-sectional study (Chapter 5) suggests that it would be unlikely that I would have found any significant associations had I investigated bias pertaining to the subject of the health threat in the prospective cohort study.

I found little evidence that parent or child personal and clinical characteristics were associated with re-vaccination. Only parent age was associated with re-vaccination intention and behaviour, with parents aged thirty-five to forty-four years being more likely to re-vaccinate their child compared to those aged eighteen to thirty-four years. However, these results should be taken with caution as analyses were likely to lack power due to small cell counts. Child personal and clinical characteristics have been investigated with relation to child influenza

vaccine uptake in the UK, however, parental factors have not been investigated (62, 458). This is surprising given that parents make the decision as to whether to vaccinate their child and would ultimately be the target of vaccine communications or interventions to increase vaccine uptake.

7.4 Factors associated with parental perception of side-effects from the child influenza vaccine

Although symptoms were once thought to be linearly related to pathology, there is now good evidence for the role of psychological factors in subjective symptom perception (227, 228). However, the influence of psychosocial factors on parental perception of symptoms in one's child have been poorly investigated (Chapter 3). Research into the provenance of parental perception of side-effects from vaccination may provide a novel approach for communications and interventions aiming to increase vaccination uptake.

Clinical trial data indicate that approximately 40% to 50% of children vaccinated with Fluenz Tetra will report side-effects (77, 78). I observed similar rates of side-effect perception in my studies, with 52.8% parents reporting side-effects in my cross-sectional study (Chapter 5) and 43.2% reporting side-effects three days after vaccination in my cohort study (Chapter 6). Recall of side-effects diminished over time, with 36.0% parents reporting that their child experienced side-effects when asked one month after vaccination (Chapter 6).

I used a cross-sectional study (Chapter 5) and a prospective cohort study (Chapter 6) to investigate factors associated with parental perception of side-effects from the child influenza vaccine. A limitation of the cross-sectional study is that I was unable to determine the causal direction of the associations between psychological factors and parental perception of side-effects. The strength of prospective longitudinal evidence over retrospective cross-sectional evidence has been considered when discussing psychological factors associated with parental side-effect perception.

The strongest predictor of parental perception of side-effects in my prospective cohort study, both three days and one month after vaccination, was the pre-vaccination expectation that the child would develop side-effects (Chapter 6,

Hypothesis 4.3.2). The role of expectation has been well-researched in subjective symptom perception, and there is good evidence that heightened expectations can cause symptoms through the nocebo response (219, 220). Symptom expectation has also been associated with perception of side-effects from medication (236, 250-252). However, to the best of my knowledge, no other studies have investigated the effect of expectation in perception of symptoms in someone other than oneself. While it is unlikely that parental expectations influence child side-effect experience, heightened pre-vaccination expectations may increase the likelihood of parents detecting and reporting side-effects. As symptom expectations are thought to arise in part from prior symptom experience (237, 264, 462), the potential for a vicious cycle exists here. The expectation that the vaccine causes side-effects may heighten perception of side-effects, which in turn may further strengthen the expectation that the vaccine causes side-effects.

Not only was parental expectation associated with side-effect perception, it also mediated the relationship between certain other psychological factors and parental perception of side-effects (Hypothesis 4.3.15). The effect of verbal suggestions of side-effects from the media and the NHS vaccination leaflet on side-effect perception three days after vaccination was mediated by expectation, as was the effect of parents' perceptions of their child's sensitivity to medicines before vaccination and side-effect perception one month after vaccination (Chapter 6). These results imply that a suggestion of symptoms, and heightened perceived vulnerability to symptoms, influence symptom expectations. Previous research has established that verbal suggestions of symptoms and increased perceived sensitivity to medicines are associated with increased subjective symptom perception (249, 254, 275, 276, 384), most likely as a result of the nocebo effect. However, my research is the first to indicate that the nocebo-like phenomenon can occur in someone other than oneself, with expectation influencing symptoms perceived in others.

Another factor implicated in parental perception of side-effects is parental anxiety (Chapter 3). Although other studies have found an association between parental anxiety and perception of symptoms in the child, these studies investigated parental perception of somatic complaints (373) and pain (352, 353, 367, 370-372) in the child. My prospective cohort study was the first to investigate the

effect of parental psychological traits on perception of vaccination side-effects in the child. I found evidence for an association between parental anxiety and side-effect perception at one month, but not three days, after vaccination (Chapter 6, Hypothesis 4.3.8). There is some evidence that anxious individuals are less likely to endorse the belief that vaccination is safe (463). This may bring about parental perception of side-effects by increasing expectations that the vaccine causes side-effects. As well as increasing parental detection and reporting of symptoms, parental anxiety may also have increased child symptom experience as a result of parental modelling and reinforcement of symptomatic behaviour and child predisposition to manifest symptoms in the presence of stressors, as well as increased (367, 371-373).

There was little evidence for a role of other parental psychological traits in side-effect perception (Hypothesis 4.3.9, Hypothesis 4.3.10, Hypothesis 4.3.12, Hypothesis 4.3.13, Chapter 6). This mirrors findings from my systematic review of psychological factors associated with parental symptom perception (Chapter 3). The only exception was the association between pessimism and increased side-effect perception one month, but not three days, after vaccination (Hypothesis 4.3.11, Chapter 6). This finding is in line with research indicating that pessimism is associated with the nocebo response (306) and that pessimism is more strongly associated with symptom recall than immediate symptom perception (464).

Parental interpretation biases may also be implicated in the perception of side-effects, with biases pertaining to the source of the health threat (man-made or naturally-occurring) being particularly influential (Hypothesis 4.3.14). I found some evidence for an association between parental interpretation biases and side-effect perception in my prospective cohort study (Chapter 6). While parents who did not report side-effects one month after vaccination interpreted man-made health threats more positively than naturally-occurring health threats, parents who did report side-effects interpreted man-made and naturally-occurring health threats as equally negative (Chapter 6). These results suggest that a tendency to interpret man-made health threats negatively is associated with parental perception of side-effects. There was no association between bias and side-effect perception three days after vaccination (Chapter 6). Therefore, negative biases for

man-made health threats may be particularly influential in parental recall of side-effects from vaccination. It was notable that the results of the larger cross-sectional study did not support an association between interpretation biases and side-effect perception (Chapter 5).

Interpretation biases pertaining to the source of the health threat, in particular man-made health threats, are consistent with factors in the wider literature which have been found to be associated with symptom perception. Interpretation biases are thought to cause and maintain worry (449) and there is good evidence that worry about man-made health threats is associated with symptom perception in oneself (278-281) and one's child (248). This lends support to the notion that threat appraisal may be influenced by underlying information processing biases, acting as a mechanism underlying parental side-effect perception. However, further research is needed to substantiate this theory.

General beliefs and attitudes may also play a role in parental side-effect perception (Hypothesis 4.3.6, Hypothesis 4.3.7). To the best of my knowledge, no other studies have investigated the association between parental beliefs and attitudes and symptom perception in the child (Chapter 3). I found evidence in my cross-sectional study that uncertainty-related beliefs, such as believing the vaccine had not been tested enough and feeling that you did not know enough about the vaccine, were associated with parental side-effect perception (Chapter 5). I also found evidence in my prospective cohort study that feeling that you did not know enough about the vaccine was associated with recalling side-effects from the child influenza vaccine one month after vaccination (Chapter 6). While I investigated associations between other beliefs and attitudes and parental side-effect perception in my prospective cohort study, data were skewed, leading to small cell counts. Thus, results should be interpreted with caution. My research did not directly test how uncertainty-related beliefs may lead to increased symptom reporting. However, it is possible that in uncertain or ambiguous situations, there is more scope for parents' pre-existing biases to come into play. Given the tendency for parents to view man-made health threats negatively, and the association between negative interpretation bias and parental perception of side-effects (Chapter 5, Chapter 6), this may lead to increased detection of vaccine side-effects. Other beliefs and attitudes were also associated with side-

effect perception in my cross-sectional study (Chapter 5) but not my prospective cohort study (Chapter 6). Thus, evidence for their role in parental side-effect perception is weaker and I have not discussed them in detail here.

I also investigated whether beliefs about medicines, perceived sensitivity to medicines and worries about aspects of modern life and their impact on health were associated with parental symptom perception (Hypothesis 4.3.3, Hypothesis 4.3.4, Hypothesis 4.3.5). In line with findings that increased perceived sensitivity to medicines was associated with subjective symptom perception following vaccination (249, 276), parents who thought their child was more sensitive to medicines were more likely to report perceiving side-effects one month after vaccination (Chapter 6). I found no evidence for a role of general negative beliefs about the harm and overuse of medicines in parental side-effect perception, despite other research finding an association with increased side-effect expectations from a hypothetical medication (272). I also found no evidence for an association between modern health worries and parental side-effect perception (Chapter 6), despite research suggesting that modern health worries are associated with subjective symptom reporting in everyday life (278-281) and following an exposure (247, 248). This pattern of results suggests that vaccine-specific beliefs and attitudes are more influential in parental perception of side-effects from vaccination than general medication beliefs.

The misattribution of existing symptoms has been associated with experiencing symptoms from a sham medication (220) and perceiving side-effects in oneself immediately following a travel vaccination (249). However, I found no evidence that parents who reported symptoms in their child immediately before vaccination were more likely to perceive side-effects from the child influenza vaccine (Chapter 6, Hypothesis 4.3.1). One recent randomised-controlled trial also found no evidence for an association between pre-existing symptoms and attribution of symptoms to a sham medication after controlling for medication beliefs and perceived sensitivity to medicines (465). Therefore, vaccine-specific beliefs and attitudes may play a more important role in parental perception of side-effects from vaccination than misattribution of existing symptoms.

I also used the prospective cohort study to investigate whether parents' perceptions of how sensitive their child was to medicines and their trust in healthcare workers changed after vaccinating their child for influenza. In particular, parents who perceived side-effects from vaccination might have thought their child was more sensitive to medicines and had less trust in healthcare workers. While parents' perceptions of how sensitive their child was to medicines did increase after perceiving side-effects from vaccination, there was no effect on parental trust in healthcare workers (Chapter 6). However, results should be taken with caution as this association was no longer significant when taking into account the effect of clustering by primary care. If associated, the potential for a vicious circle could exist here, with parents who believe their child is more sensitive to medicines, perceiving more side-effects in their child, which further heightens their perception of how sensitive their child is to medicines.

Although not a central aim of this thesis, I also investigated whether parent or child personal and clinical characteristics were associated with parental perception of side-effects from vaccination. Contrary to previous research which indicates that females are more likely to perceive symptoms in themselves than males (269, 297, 302, 331), I found that female parents were less likely to report side-effects in their child than males in my cross-sectional study (Chapter 5). A comprehensive systematic review of factors associated with the nocebo effect found 'very little' evidence for the role of gender in the nocebo effect (220), and research published since has suggested that males may be more likely to perceive symptoms from sham medications (465). I found no evidence for an association between parent gender and parental side-effect perception in my prospective cohort study (Chapter 6). To the best of my knowledge only one other study has investigated the effect of parent gender on parental side-effect perception from vaccination, also finding no association (466, 467).

I also found evidence in my prospective cohort study that parents were more likely to perceive side-effects in their male child, rather than female child, one month after vaccination (Chapter 6). It is not clear why this was. There was no evidence for an association between child gender and parental perception of side-effects three days after vaccination (Chapter 6) or in my cross-sectional study (Chapter 5). Whether these findings are replicable remains to be seen.

Previous studies indicate that parents who have a history of, or who are currently experiencing, similar symptoms to those being investigated in their child report increased perception of symptoms in their child (344, 355, 373, 468-470). Likewise, parents who think their child has previously experienced symptoms are also more likely to perceive symptoms in their child (344, 350, 351, 355, 370-372). I found evidence for an association between child chronic illness and parental side-effect perception in my cross-sectional study (Chapter 5), but not my prospective cohort study (Chapter 6). The lack of evidence for an association in my study could be due to the mild and transitory nature of side-effects from the child influenza vaccine (73), compared to the more chronic nature of the symptoms investigated in the previous literature. Increased parental perception of side-effects in children with chronic illnesses may be due to the parental perception that the child is vulnerable. In line with this notion, I also found evidence that parents of first-born children were more likely to perceive side-effects from the child influenza vaccine (Chapter 5). However, I found no evidence for this association in my prospective cohort study (Chapter 6).

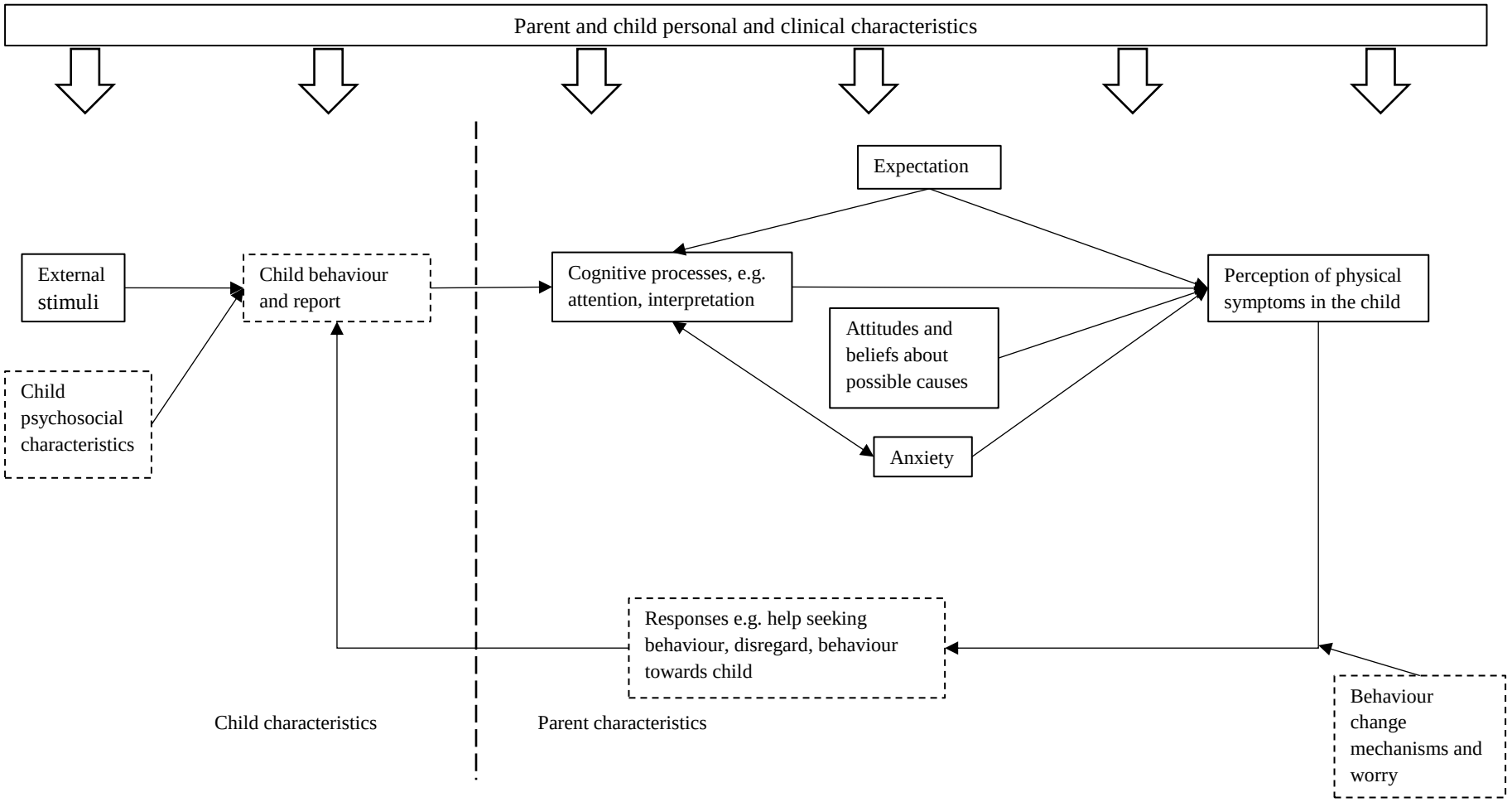
I also found evidence in my cross-sectional study that older parents were less likely to perceive side-effects in their child (Chapter 5); I found no evidence for this association in my prospective cohort study (Chapter 6). Older parents may be more likely to have had other, older children and so may have been less likely to perceive side-effects from vaccination in the index child. Other studies have also found no association between parent age and symptom perception (355, 357, 358, 361).

7.4.1 A model of parental perception of symptoms

There is good evidence that psychological factors influence parental perception of side-effects from vaccination. While multiple models exist which attempt to describe subjective symptom perception (233), there are no models describing symptom perception in others. This is probably due to the dearth of research and lack of comprehensive reviews investigating factors associated with symptom perception in someone other than oneself. However, the ability to perceive symptoms in others has important consequences, particularly for parents who are in charge of treatment decisions for their child. With this in mind, I have proposed a model of parental symptom perception based on research investigating

symptom perception in one's child and oneself (see Figure 10). Factors that I did not investigate in my theses are outlined using dotted lines.

Figure 10. Model of parental symptom perception



For parents to perceive symptoms in their child, they must attend to their child's behaviour and interpret behavioural cues as the child experiencing a symptom. This can occur in the presence or absence of an exposure such as vaccination. If and how a child expresses that they are experiencing a physical symptom may depend on the child's psychosocial characteristics, such as their temperament. A child's ability to verbalise their bodily sensations will also depend on their age and health status.

Expectation is likely to play a key role in parental perception of symptoms, directly influencing parental symptom perception as well as parental cognitive processes. Expectation could arise from receiving verbal suggestions that symptoms are likely, seeing others experiencing symptoms in the same or similar situations, or having previously experienced symptoms in the same or similar situations.

While trait negativity has been implicated in models of subjective symptom perception (233), my research found that parental anxiety played a stronger role in symptom perception in one's child than trait negativity (Chapter 3, Chapter 6). Anxiety is associated with increased attention to negative stimuli (471) and negative interpretations of information (472). It is therefore likely that parental anxiety is associated with parental cognitive processing of the child's behaviour.

Parents' reactions to a symptom, for example seeking help from a medical practitioner, are likely to be modified by a range of factors which influence behaviour change, such as capability, opportunity and motivation described by the behaviour change wheel (473). For example, a parent may be less likely to seek help if they are ill themselves and so lack the ability to take their child to visit a health professional (capability); if they do not have access to a mode of transport to take their child to visit a health professional (opportunity); or if they do not foresee any positive impact of taking their child to visit a health professional (motivation). Increased worry may also influence help-seeking behaviour. Parental behaviour, such as giving the child medication or seeking medical attention, may bring about further changes in the child's behaviour and self-report of symptoms.

Parent and child personal and clinical characteristics may affect parental symptom perception at all stages of the process. For example, parents may feel that their young child or first child is more vulnerable to illness, causing parents to selectively attend to their child's behaviour and interpret cues as indicative of physical symptoms. Clinical characteristics, such as a history of symptoms in the parent (344, 373, 468) or child (344, 370-372) are also associated with increased symptom perception. Parent or child history of a symptom may increase parental symptom expectation, increasing attention to indicators of that symptom and causing parents to interpret cues as the presence of that symptom.

To the best of my knowledge, this is the first model describing parental symptom perception. It could also be extended to symptom perception in others more generally. One key difference to models of subjective symptom perception is that in oneself, a bodily sensation interpreted as a symptom may cause anxiety or stress, which may cause further bodily sensations such as an increased heart rate or sweaty palms. These sensations would then be interpreted as further signs of illness (235). In parental symptom perception, this physiological feedback cannot exist as information about child symptoms comes from external cues.

7.5 Implications and recommendations

As we have seen, psychological factors are associated with child vaccine uptake and parental perception of side-effects from vaccination. But what are the ramifications of these findings? Based on the results of my thesis and the wider literature I have made several recommendations for vaccine communications and future research.

The recommendations I have made are specific to the child influenza vaccine, but many could generalise for use in communications and research about other vaccines. However, care needs to be taken when extrapolating guidance to other vaccines, to ensure that nuances relevant to individual vaccinations are taken into account. For example, whether the media furore over MMR in recent years (474, 475) or the peculiarities of the HPV vaccination, with parental concerns influenced by complex underlying attitudes towards sex (476), require a qualitatively different approach is unclear.

7.5.1 Perception of adverse effects from vaccination

Public health communications and interventions aim to increase vaccine uptake. To be maximally effective, messages to parents should target perceptions that are both amenable to change and strongly associated with vaccine uptake. Evidence from my systematic review of factors affecting vaccine uptake in young children (Chapter 2) and cross-sectional study (Chapter 5) indicated that parental perception that a vaccine causes adverse effects and parental fear or concern about potential adverse effects was strongly associated with vaccination uptake. My results highlight the importance that parents place on perceiving side-effects from vaccination and demonstrate that the perception of side-effects is susceptible to influence from psychological factors. By reducing parental perception of side-effects from vaccination, vaccination intention and initial uptake may increase. This is a novel target for public health communications and vaccine intervention research.

I investigated associations between psychological factors and parental perception of side-effects in my cross-sectional (Chapter 5) and prospective cohort study (Chapter 6). Parents' pre-vaccination expectations that the vaccine would cause side-effects were strongly associated with later perception of side-effects in my prospective cohort study (Chapter 6); I did not investigate this factor in my cross-sectional study. My results suggest that parental perception of side-effects could be reduced by decreasing parental expectations that the vaccine causes side-effects (Chapter 6). Mediation analyses indicated that suggestion of side-effects from the media and the NHS vaccination leaflet affected parental perception of side-effects through expectations (Chapter 6). Therefore, parents' side-effect expectations could be minimised by decreasing the suggestion that the vaccine causes side-effects in information disseminated by influential sources, such as the NHS vaccination leaflet. Despite their obligation to inform patients about adverse effects of medication, these sources should aim to minimise their suggestion of the incidence of side-effects as much as possible. Although the ethical implications of decreasing parental expectations of side-effects need to be considered, so too do the implications of causing parents to consistently overestimate the likelihood of side-effects from vaccination.

I investigated how current phrasing used in vaccine communications was understood by a nationally-representative sample of 1001 parents of children eligible for the child influenza vaccine (Chapter 5). In line with other research (272), I found that current phrasing describing the incidence of side-effects from vaccination was associated with substantial overestimation of the likelihood of side-effects (Chapter 5). Overestimation of the incidence of side-effects likely impacts treatment decisions and medicine adherence (402, 403) as well as causing unnecessary symptoms through the nocebo phenomenon (220). Changing how side-effect information from influential sources, such as the NHS vaccination leaflet, is presented might bring parental expectations in line with more accurate estimates of the incidence of side-effects.

While there is good evidence that worry about side-effects is associated with initial vaccine uptake (91, 93)(Chapter, 2, Chapter 5), I also investigated the implications of parental perception of side-effects from the child influenza vaccine on intended and actual re-vaccination in my cross-sectional study (Chapter 5; only intention investigated) and prospective cohort study (Chapter 6; intention and uptake investigated). There was some evidence that parental perception of side-effects, increasing severity of side-effects perceived and worry about side-effects was negatively associated with re-vaccination intention (Chapter 5, Chapter 6) and actual re-vaccination behaviour (Chapter 6). Therefore, providing reassurance to parents about the typically transitory and non-harmful nature of side-effects (73) may be a useful strategy in increasing initial vaccine uptake, as well as potentially reducing long-term attrition among parents who have previously vaccinated their child. However, results should be taken with caution as there was no longer a significant association with actual re-vaccination when accounting for clustering by primary care practice (Chapter 6). In spite of this, due to the wide-scale nature of the child influenza vaccine programme, if a factor exerts even a small positive effect on vaccination intention or uptake, this could have greater consequences on a nationwide scale.

One way to reduce side-effect expectations could be to make subtle changes to the wording of side-effect information in patient information leaflets for vaccinations and other official vaccine communications. Positive framing of side-effect information has been shown to successfully decrease side-effect

expectations and experience. For example, one study aiming to increase influenza vaccine uptake in 'at risk' adults who had never previously been vaccinated, investigated the effect of framing side-effect information positively, as the percentage of people who did not experience side-effects from vaccination and remained influenza free, or negatively, as the percentage of people who did experience side-effects from vaccination and who went on to experience influenza (477). Although there was no difference in rates of uptake, those in the positive framing condition had more realistic, lower expectations of vaccine side-effects and experienced fewer side-effects (477). Another recent randomised-controlled trial also found that fewer participants attributed side-effects to a sham medication when side-effect information was framed positively in the patient information leaflet (478). There was no scope to investigate the effect of positive framing on uptake of the child influenza vaccine in the studies included in the thesis. Using results from the thesis, this could be a next step for research aiming to increase uptake of the child influenza vaccine.

One issue worth noting is that adding more information about vaccine side-effects to vaccine communications may raise parents' expectations that the vaccine causes side-effects. However, if the addition is short and does not talk about the incidence of side-effects, or replaces redundant text currently being used, it should not raise parental expectations. The 'protecting your child against flu' vaccine leaflet currently states that 'children may develop a runny or blocked nose, headache, general tiredness and some loss of appetite. However, these are much less serious than developing flu or complications associated with flu' (479). This does not give parents an indication of how long side-effects may last, nor does it tell parents that vaccine side-effects are usually harmless. Information published online by the NHS states that the side-effects 'linked with the flu nasal spray vaccine are almost always mild and short-lived' (401). This sentence could be added to the 'protecting your child against flu' leaflet, while the sentence comparing the severity of symptoms from influenza and the vaccine could be removed.

Altering how side-effects are framed in the patient information leaflet and communications by Public Health England and the NHS could be an easy, effective and far-reaching way of reducing parental expectations about side-

effects from vaccination and later perception of side-effects from vaccination. There would be no cost implications of altering side-effect information (478) and this intervention would be in line with recent legislation stating that all potential risks from medications should be disclosed to patients (480). Research also indicates that leaflets which employ positive framing of side-effects are as credible as those which are negatively framed (478).

7.5.2 General beliefs and attitudes

Very little research has focused on comparing the efficacy of messages to determine which are most beneficial in increasing vaccine uptake (179). Where studies do exist, outcomes are often proxy measures such as vaccination intention or attitudes, rather than vaccine uptake (179, 481). A recent review of the literature on vaccine interventions found that interventions which induced more positive vaccine beliefs; influenced social norms associated with vaccination; and reduced barriers to motivation and facilitated actions through reminders and prompts, increased vaccine uptake (179). These map on to theoretical constructs of attitudes, subjective norms and perceived behavioural control which are thought to underpin health behaviours (87, 88, 418). Multiple negative vaccine beliefs and attitudes were associated with vaccine uptake in my cross-sectional study (Chapter 5), suggesting them as possible targets for future vaccine communications and intervention research. As this study was conducted on a sample of nationally-representative parents of children eligible for the child influenza vaccine, the strength of the evidence is good. However, due to the cross-sectional and retrospective nature of the study, I am unable to conclude whether there is a causal influence of parental beliefs and attitudes on vaccine uptake.

Beliefs which exerted strong effects on vaccine uptake included feeling that the vaccine was safe and effective (Chapter 5); communications could promote these beliefs. This may be easier said than done, however. The term ‘vaccine effectiveness’ is poorly understood, with only 19% of parents correctly interpreting the meaning of the hypothetical statement that the ‘child flu vaccine is 50% effective’ (Chapter 5). Vaccine effectiveness should be more clearly described in communications. Communications should explain that the effectiveness of the vaccine is related to their child’s risk of catching influenza.

For example, communications could state that ‘everyone’s individual risk of catching flu varies depending on many different factors. The effectiveness of the vaccine relates to how much the risk of *your child* catching flu is reduced after they are vaccinated.’ Pictograms could be used to help illustrate this case further (482).

One finding from my systematic review of factors associated with vaccine uptake was that vaccination was more often associated with parents’ perception of how susceptible their child was to the illness (nine of twelve studies found), than with how severe parents thought the illness would be for the child (five of fifteen studies found; Chapter 2). This indicates that future communications should focus on children’s susceptibility to the illness over illness severity. In my cross-sectional study, I also found evidence that parents who believed that their child was susceptible to influenza or that influenza would be a serious illness for their child were more likely to have vaccinated their child in 2015/16 and to intend to vaccinate their child in the 2016/17 influenza season (Chapter 5). The current 2018/19 ‘protecting your child against flu’ leaflet does not mention that children are susceptible to influenza (479). Instead it states that ‘having the vaccine will help protect your child from what can be a very nasty illness in children. Children under the age of five have the highest rate of hospital admissions due to flu’ (479). Based on my work, adding a sentence that states that ‘children have a high risk of catching flu as they come into contact with lots of people each day and have poor hand hygiene’ may be warranted.

Efforts must be made to ensure that interventions are easily accessible to the general population, for example using simple language. Easily implementable interventions, such as changing the wording of existing information and communications about vaccination, are likely to be particularly attractive options. Recently, there has been a rise in interventions delivered through mobile phones (mHealth) and the internet (eHealth). These are likely to be particularly good targets for vaccine interventions as they are accessible to most, with 85% adults in the UK owning a smartphone (483). Electronic interventions also have the added benefit of being able to tailor messages based on parents’ specific concerns about vaccination. Systematic review evidence indicates that media such as mobile phone applications have great potential for improving vaccination uptake

(484). While not it was not in the scope of this thesis to investigate the influence of interventions, electronic or otherwise, on vaccine uptake and parental side-effect perception, this could be a direction for future research.

Social media might also be a particularly important target for novel interventions. One recent study compared the use of a website with vaccine information, a website with vaccine information plus additional interactive social media components and usual care on parental attitudes about vaccination and vaccine uptake for a number of routine child vaccinations, not including influenza (485, 486). Parents who were vaccine hesitant during pregnancy and who were assigned to either website condition showed a significant amelioration of vaccine attitudes compared to usual care (485). Children of parents assigned to use the website with the additional interactive social media component were more likely to be vaccinated on time and to be up-to-date on their vaccines at age 200 days compared to usual care; there was no evidence for an effect in children of parents who used the vaccine website with no additional social media component (486). Interventions which make use of social media may work by influencing parents' social norms: a factor implicated in theories of behaviour (88) and which has been identified by a recent review of vaccine interventions as being particularly effective at increasing vaccine uptake (179).

When deciding whether to vaccinate their child, parents often consult multiple sources for advice, such as their friends and family, healthcare providers and information published online by official and non-official sources (487). Given that we know that people will be exposed to multiple messages about the vaccine from different sources, an important question to ask is how do we make sure that parents treat official communications as true? Inoculation theory posits that attitudes can be inoculated against persuasion (488) and suggests that two components bring about resistance to other attitudes: the recognition that one is vulnerable to threat, and raising and discrediting counterarguments (489). Phrasing official vaccine communications in this way may make induced positive vaccine beliefs and attitudes more resistant to change; this could be investigated by future research.

There is also much evidence indicating that people prefer messages that are in line with their own beliefs, often discounting information which is incongruous as being unimportant or not relevant to oneself (490). This is also known as defensive processing or bias and is thought to happen when the message threatens one's sense of self (491, 492). In the context of child vaccination, this might mean that parents who are not in favour of child vaccination could refute information in which vaccines are presented positively without engaging with it. So how could we increase the receptivity of these parents to health messages about the benefits of vaccination and the dangers of vaccine-preventable diseases? One option could be self-affirmation, in which people reflect on values, attributes, and past behaviours important to themselves, reinforcing one's sense of self-integrity and adequacy (493). Reaffirming self-worth is thought to protect self-integrity, reducing defensive bias and allowing threating information to be processed (494). In line with this theory, self-affirmation is associated with acceptance of messages about health threats, and positive behaviour intention and behaviour change (495, 496). Many different methods have been used to manipulate self-affirmation. However, they often involve burdensome tasks such as writing about why a particular value is important; these tasks would be difficult to include in widespread vaccine communications (497). Nevertheless, some studies have successfully induced self-affirmation using less intensive manipulations (e.g. (498, 499)). To the best of my knowledge, there is only one study investigating the manipulation of self-affirmation on child vaccine uptake. In this study, parents who self-affirmed had lower vaccination intentions and were more likely to believe that the MMR vaccine caused side-effects (500). Therefore, the use of self-affirmation to increase vaccination should be approached with caution. However, better quality research is needed to see whether these results are replicated with other types of manipulations of self-affirmation which would be more suited to inclusion in national vaccination campaigns, such as including a phrase stating that 'we know that you are doing your best for your child,' and different vaccines.

7.5.3 Knowledge

Vaccine interventions often aim to increase parents' knowledge about vaccines. I investigated whether feeling that parents' perception that they did not know

enough about the vaccine was associated with child influenza vaccine refusal in my cross-sectional study (Chapter 5). Parents who felt that they did not know enough were less likely to vaccinate their child in 2015/16 and less likely to intend to vaccinate their child in 2016/17. These results suggest that increasing parental knowledge about influenza and the child vaccine might increase uptake. In my cross-sectional study, approximately 5% and 15-25% of participants answered belief and attitude items as 'don't know' and 'neither agree nor disagree' respectively (Chapter 5). This suggests that a substantial proportion of the public are willing to admit their lack of knowledge about influenza and the child vaccine and may be open to new information.

While outside the scope of this thesis, other research investigating the effect of increasing parental knowledge about vaccines and vaccine-preventable illnesses gives mixed results. For example, a recent comprehensive systematic review of randomised-controlled trials found low- to moderate-certainty evidence that face-to-face educational interventions increase vaccine uptake (501). Similarly, a recent summary of interventions to tackle vaccine hesitancy indicated that educational interventions yield mixed results: some studies found a positive influence of increased knowledge on vaccine intentions, attitudes and uptake, while others found no change or a worsening of intentions (481). One reason why interventions increasing parental knowledge may not be successful in increasing vaccine uptake is that vaccination is a complex behaviour which depends on many factors. One influential theory of behaviour change, the behaviour change wheel, has identified nine intervention functions, including persuasion, incentivisation, enablement and modelling, which should be targeted to bring about behaviour change (473). Interventions which target multiple behaviour change techniques may be more successful in increasing vaccine uptake.

In addition to identifying messages which could be targeted by vaccine communications and vaccine interventions, my research also identified other issues which might hinder uptake of the child influenza vaccine in England. One example is poor vaccine-eligibility knowledge by both parents and healthcare practitioners. Almost one-third of parents of vaccine-eligible children in my cross-sectional study did not know their child was eligible for the child influenza vaccine in 2015/16, or incorrectly thought that their child was not eligible

(Chapter 5). In my systematic review of vaccine uptake, there was good evidence that incorrect knowledge, confusion, or difficulty remembering the vaccine schedule was associated with not vaccinating the child (six of seven studies found; Chapter 2). In healthcare practitioners, incorrect vaccine-eligibility knowledge may mean that vaccine-eligible children are denied vaccination. In the 2016/17 influenza season, children aged two, three and four years on 31st August 2016 (i.e. birth dates between 1st September 2011 and 31st August 2014) were eligible for vaccination through their primary care practice (502). As the influenza season progressed, some of these children turned five but were eligible for the vaccine, while other children born on or after 1st September 2014 turned two but were not eligible for vaccination. During recruitment for my prospective cohort study, I informally observed the misinterpretation of vaccine-eligibility guidelines. Some primary care practices interpreted guidelines to mean that children should be aged two, three or four years on the day of vaccination. Thus, I saw some children who were aged five and were eligible for the vaccine, being refused vaccination. Better communication to practitioners, as well as parents, may be required.

7.5.4 Anxiety

While not investigated with relation to vaccine uptake in this thesis, one factor which is unlikely to be changed by vaccine communications, but which may be important to keep in mind when thinking about child vaccine uptake, is parental trait anxiety. Anxiety is characterised by excessive worry (377). Worry, in particular about possible adverse effects of the vaccine, is strongly associated with child vaccination refusal (91, 95, 270) and increased subjective symptom perception (247, 248, 278-281). I investigated the association between parental trait anxiety and parental perception of side-effects in my prospective cohort study, finding evidence of an association with parental recall of side-effects from the child influenza vaccine one month after vaccination (Chapter 6). This evidence suggests that minimising parental concern about potential adverse effects of vaccination and fostering the belief that vaccination is safe may reduce the number of parents recalling side-effects from the child influenza vaccination. However, further research is needed to characterise the role of worry and anxiety in vaccine uptake and side-effect perception.

7.5.5 Vaccine recommendations from a healthcare provider

In my systematic review of vaccine uptake in young children I found good evidence that receiving a vaccine recommendation from a healthcare professional was associated with uptake of child vaccinations (eight of nine studies found an association; Chapter 2). Another narrative review has also identified that receiving a recommendation from a healthcare provider that one's child should be vaccinated is strongly associated with vaccine uptake (179). Despite being unable to infer causality due to its cross-sectional nature, I also found that receiving a vaccine recommendation from a healthcare provider was associated with uptake of the child influenza vaccine in my cross-sectional study (Chapter 5). While all healthcare providers are encouraged to provide strong vaccine recommendations (503, 504), data indicated that almost half of participants disagreed that a health professional had recommended vaccination (Chapter 5). In conducting my prospective cohort study, I also informally found that multiple primary care practices did not send vaccine invitations to parents of vaccine-eligible children. This is in spite of guidance stating that primary care practices should 'ensure that they are making every effort to identify and contact eligible patients' (503). New best practice guidance for primary care practices states that personalised invitations should be sent to parents of vaccine-eligible children and that multiple contact should be made 'until the child is immunised or an active refusal is received' (504). However, whether primary care practices follow guidance is not regulated.

7.5.6 Practicalities

Other factors which may hinder uptake of the child influenza vaccine relate to practicalities associated with child vaccination. In my systematic review of factors associated with uptake of child vaccinations, I found good evidence that practicalities such as perceived logistical barriers and inconvenient appointment locations or times, were associated with not vaccinating the child (five of seven studies found; Chapter 2). One such practicality which affects child influenza vaccination and which has influenced recent vaccination recommendations is the location of delivery of the vaccine. National uptake rates indicate that vaccination is consistently higher in children who are vaccinated in school (approximately 52% to 61% vaccinated), compared to those vaccinated at their primary care

practice (approximately 30% to 44% vaccinated) (15, 56-59). This is likely due to the relative ease for parents of school vaccination. As such, recommendations were updated for the 2017/18 influenza season, with children in school year reception being offered vaccination in school (503). For parents of young children offered vaccination in the primary care practice, making vaccination as easy as possible, for example by holding evening and weekend vaccination clinics, will likely help increase vaccination rates (505).

7.5.7 Interpretation bias

Although information processing biases can be modified, it is unlikely that short vaccine communications will alter parents' interpretation biases. I investigated whether parental negative interpretation biases were associated with vaccine uptake, intention and side-effect perception in my cross-sectional (Chapter 5) and prospective cohort study (Chapter 6). Results were mixed. I found evidence for an association between parental negative biases pertaining to the source of the health threat (naturally-occurring or man-made) for vaccine uptake in 2015/16 and vaccination intention for 2016/17 in my cross-sectional study; there was no association between bias and parental perception of side-effects (Chapter 5). There was no association between parental negative interpretation biases pertaining to the subject of the health threat (self-relevant or child-relevant). In contrast, I found no association between parental negative interpretation biases pertaining to the source of the health threat and re-vaccination intention or uptake in my prospective cohort study, while finding some evidence for an association between parental bias and recall of side-effects one month after vaccination (Chapter 6). Due to the mixed nature of results, interpretation is difficult. Further research, powered to detect small effects, is needed to substantiate whether parental interpretation bias is associated with vaccination behaviour. Some tentative suggestions might be made from my results, however. For example, my results suggest that attempts should be made to remove ambiguity and uncertainty from communications, to avoid negative interpretations from those with negative biases. However, it is difficult to remove all ambiguity surrounding the child influenza vaccine, as parents will likely receive conflicting information from different sources such as their friends and family, the media, social media and official communications (487).

If substantiated by further research, investigating potential associations between parental interpretation biases and vaccination behaviour is the first step in designing an appropriate intervention to modify underlying biases. Although current cognitive bias modification techniques are inappropriate for widespread vaccine communications, the notion that interpretation biases may play a causal and maintaining role in maladaptive behaviours (192) and worry (449) makes the notion of modifying such biases an interesting prospect. In cognitive bias modification studies, behaviour and information processing biases are measured, after which participants complete cognitive bias modification tasks. Biases are then measured again, to ascertain whether biases were successfully modified. Behaviour is also measured again, to see whether bias modification has had any influence. Studies which employ cognitive bias modification techniques often do so in an attempt to prove the causal influence of cognitive biases on behaviour.

While cognitive bias modification has been successful for some outcomes, such as ameliorating the symptoms of anxiety (201, 506) and eating disorders (507), few studies have investigated the role of cognitive bias modification on public health behaviours. Where studies have investigated the effect of cognitive bias modification on public health behaviours, they yield mixed results. A recent meta-analysis investigating cognitive bias modification in relation to smoking and alcohol problems found that while there was a moderate effect on cognitive bias, modification had no effect on addiction behaviour (508). This caused authors to call into question the 'clinical utility of cognitive bias modification as an intervention for addiction problems' (508) (p. 2/19). However, when studies investigating bias modification in alcohol disorders were re-analysed taking into account differences in study methods and populations, researchers found that modification influenced drinking behaviour in the short-term but not long-term (e.g. three months, but not six months) (509). Of the studies reviewed, only one attempted to modify interpretation bias; all other studies investigated attention bias, approach bias and response inhibition. This study found that while interpretation bias modification was successful in changing alcohol-related biases in a group of male students with hazardous drinking behaviour, there was no effect on alcohol consumption (510).

Other studies have investigated the effect of cognitive bias modification on different public health behaviours, also yielding mixed results. For example, one study found that interpretation bias modification in undergraduate students was associated with increased spending on sun cream in a virtual task, but was not associated with intention to adopt sun protective behaviours (511). Results of this study should be taken with caution as, to the best of my knowledge, no research exists investigating whether there is an underlying association between interpretation bias and sun protective behaviours, nor was adoption of sun protective behaviours measured before the bias modification task. Attention bias modification has been found to promote healthy eating (455).

How evidence for cognitive bias modification in behaviours such as smoking, drinking alcohol and eating unhealthy foods might translate to vaccination decisions is unknown. So far, cognitive bias modification has been used in attempts to stop detrimental habitual behaviours, but in the case of vaccine uptake, cognitive bias modification would aim to promote a one-off beneficial behaviour. Initiating and stopping behaviours are thought to be conceptually different (512), so results found in bias modification studies investigating smoking, drinking and eating unhealthy foods may not carry over to vaccination. In addition, most research investigating cognitive bias modification in public health behaviours has looked at the effect of modifying attention bias, not interpretation bias. Despite mixed evidence for the use of interpretation bias modification for uptake of public health behaviours, interpretation bias modification is thought to have a more consistent effect on target bias than attention bias modification (400) and may therefore be more likely to bring about changes in behaviour.

While interpretation bias modification may theoretically affect vaccination, the practicality of a widescale interpretation bias modification intervention is an important consideration. When completing interpretation bias modification training, participants are presented with many trials (often up to 100), which are consistently disambiguated in a negative or positive manner (negative or positive training condition respectively). When later presented with ambiguous task trials, participants tend to interpret ambiguity in the direction of training. There are many variables which may impact how successful interpretation bias

modification training is. First, the effect of multiple training sessions is unclear, with a recent review of meta-analyses indicating that two meta-analyses found an increased effect of multiple training sessions, while another found that a single session was most effective; three found no association (400). Second, the duration of cognitive bias modification training is typically short-lived, although studies indicate that training effects persist the day after training (513, 514). Third, the location of the bias modification training should be considered as cognitive bias modification is most effective when delivered in a laboratory setting (400). Outside of a research context, could cognitive bias modification be used in practice to promote vaccine uptake? Possibly. Although a small number of trials, conducted outside of a laboratory might only have a very small, short-lived effect, given that any public health intervention would be applied across the population, even a small effect that increases vaccine uptake by one or two percentage points might still be worthwhile.

While outside the scope of this thesis, investigating whether other information processing biases, such as attention bias and recall bias, may influence parental vaccination behaviour may also be valuable. For example, negatively biased parents may be more likely to attend to and recall negative information about the vaccine, such as previous side-effects that their child has experienced from vaccination. This in turn may negatively influence parents' decision to re-vaccinate their child.

7.5.8 Personal and clinical characteristics

Unlike psychological factors which can help inform the content of communications and interventions, personal and clinical characteristics associated with vaccine refusal may help identify target groups for more specific or intensive communications (95). In the case of child influenza, I identified very few associations between vaccine uptake and personal and clinical characteristics. Only parent age was associated with re-vaccination intention and actual re-vaccination in the prospective cohort study (Chapter 6); I found no evidence for associations between vaccine uptake and personal or clinical characteristics in the cross-sectional study (Chapter 5). Two other studies have investigated the impact of population-level factors on child influenza vaccine uptake in the UK. Vaccine refusal was associated with living in: more deprived areas (62, 458); urban areas

(62); areas with increasing proportions of black-ethnic and Jewish populations (62); and areas with a higher number of children living in each household (458). Studies did not investigate parent personal or clinical characteristics. More research investigating how personal and clinical characteristics impact child influenza vaccination is needed to ensure that the relative importance of psychological factors on behaviour is not overestimated.

7.6 Strengths and limitations of the thesis

The specific strengths and limitations of each component of this thesis are described in the appropriate chapters. However, some overarching factors should also be considered.

One of the main strengths of this thesis is the timeliness of the research after the introduction of the child influenza vaccine to the vaccine schedule in the UK. My thesis includes the first set of studies to investigate what parents thought about the child influenza vaccine as well as being the first to assess psychological factors associated with vaccination. To the best of my knowledge it is also the first study to provide data on re-vaccination rates for the child influenza vaccine; contact with Public Health England and NHS England has failed to uncover any official data.

Another strength is that my prospective cohort study was the first to investigate the effect of expectation on parental perception of side-effects from vaccination. Given the central role of expectation in the nocebo effect (219, 220), this is surprising. Studies have so far focused on how psychological factors may impact child symptom experience, but my thesis identifies and highlights factors which are likely to impact parental perception of symptoms. This is important in its own right due to the influence that parental perception of symptoms has on vaccination decisions and more broadly, on help-seeking behaviour and medication adherence. Parental perception of side-effects may also influence other factors, such as how sensitive to medicines parents believe their child to be (e.g. Chapter 6).

Other strengths of the thesis include the use of multiple methods, including two systematic reviews, a cross-sectional study and a prospective cohort study. Being systematic, my reviews not only covered the entirety of the literature as far as

possible, but also reduced the risk of bias associated with publication bias or 'cherry-picking.' My cross-sectional study had a large, nationally-representative sample, increasing confidence that my results would hold true in the wider population. My cohort study was conducted prospectively, lending credence to the notion that psychological factors are causally associated with parental perception of side-effects from vaccination and re-vaccination behaviour. In addition, my research was interdisciplinary, exploring vaccination, a public health behaviour, using an experimental psychology approach.

One of the primary aims of this thesis was to investigate factors associated with parental perception of side-effects. One overarching limitation of my studies is that just taking part, especially in the prospective cohort study, might have increased parents' expectations that their child would experience side-effects and reporting of side-effects. The medical setting in which parents were recruited for the prospective cohort study may have also affected side-effect perception. However, as parents were asked whether their child had experienced side-effects from vaccination in follow-up tasks which were not completed at the primary care practice, this is unlikely. Being asked about potential side-effects may have heightened parents' attention to signs of side-effects in their child and caused parents to interpret any symptoms displayed by the child as arising from the child influenza vaccine. I was unable to mitigate this in my study, which through necessity relied on self-report. These problems affect all studies in which subjective side-effects are investigated, including clinical trials (77).

Another limitation of the studies in this thesis comes from the use of self-report measures, which are open to problems such as recall errors (515). With regard to child influenza vaccine uptake, research indicates that parent-report of a child's influenza vaccine status is a robust measure (516). With regard to perception of side-effects, as I was interested in parental perception of side-effects from vaccination, I necessarily had to use a self-report measure.

In my cross-sectional and prospective cohort study, I investigated only parent-reported symptoms; whether children actually did experience symptoms is unknown. However, the investigation of factors associated with parental perception of vaccine side-effects is important in its own right. The consequences

of perceiving side-effects, such as avoiding other vaccinations or medications in the future, will occur based on parental perception of side-effects, regardless of the child's subjective experience.

Other limitations of the thesis relate to the space available for task materials in my questionnaires. Restrictions on the length of study materials meant that I was not able to investigate all potentially relevant factors in both studies. Factors with no theoretical basis for their influence on parental side-effect perception, such as child temperament, were not investigated. In addition, I was also only able to investigate interpretation bias; other biases of information processing such as attention and recall bias may also be important in parental vaccination decision-making. The retrospective nature of the cross-sectional study meant that measuring parental pre-vaccination expectations of side-effects would have been confusing for participants, so I did not investigate this factor. Similarly, I did not ask if the child had been experiencing other symptoms at the time of vaccination.

Although my studies were generally well powered to identify factors associated with child influenza vaccine uptake and parental perception of side-effects, when looking in more detail at some of the predictors, the sample size included in analyses decreased. This meant that some analyses relied on small cell counts and therefore should be interpreted with caution. In addition, I was only powered to identify medium effect sizes in my interpretation bias analyses. Only approximately one-third of participants completed interpretation bias tasks satisfactorily for inclusion in the analyses. This smaller sample size means that factors which could have exerted small, but still important, effects may have been missed.

Finally, data are correlational, and caution should be taken when interpreting results and recommendations for implementation as findings do not necessarily indicate causal influence.

7.7 Conclusions

Vaccination is one of the most successful interventions in modern medicine (517). However, uptake of the child influenza vaccine in England has been consistently low (15, 56-59). My research shows that this may be associated with the perception that the vaccine causes side-effects. However, not all side-effects

perceived from vaccination can be attributed to the pharmacological actions of the vaccine. While efforts have been made to increase vaccine uptake, they have not focused on decreasing the perception that the vaccine causes side-effects. The studies reported in this thesis reliably demonstrate that psychological factors such as parental pre-vaccination expectations, anxiety, uncertainty-related beliefs and interpretation biases play a role in side-effect perception. Current communications about vaccines are associated with considerable overestimation of the incidence of side-effects from vaccination. My results suggest that bringing parental expectations in line with more accurate estimates of the incidence of side-effects, might decrease side-effect perception and increase vaccine uptake. Decreasing parental worry about potential side-effects from vaccination might also increase vaccine uptake. This is a novel target for vaccine communications and interventions, and one which could be highly impactful. In the UK alone, sixteen children died from influenza in the 2017/18 season (59). Implementing the changes suggested in this thesis could help increase uptake of the child influenza vaccine and, ultimately, save lives.

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Appendix 1. Methods of articles included in systematic review of factors affecting vaccine uptake in young children

Citation	Study design (Methodology)	Number of participants	Inclusion criteria	Age of child	Location (time of data collection)	Vaccine/s (ascertained)	Definition of 'vaccinated'[2]	Risk of bias score
Alfredsson et al 2004 (119)	Case-control (postal questionnaire)	118	Cases (n=50) – Parents of all children born in Child Health Centres in Gothenburg in 1995 and 1996 who had not received MMR vaccine according to charts. Controls (n=68) – Parents of vaccinated children listed prior to unvaccinated children in birth register in 1996 cohort	3-5 years old	Gothenburg, Sweden (November 1999)	MMR (Child Health Centre chart review)	Vaccinated with the MMR	9
Allred et al 2005 (167)	Cross-sectional (telephone interview)	7810	Parents of children aged 19-35 months in selected urban areas of USA (selected by CDC for inclusion in NIS)	19-35 months	USA (July 200-December 2002)	DTP, MCV, Hib, hep B (verified by child's immunisation provider)	≥4 DTP, ≥3 poliovirus, ≥1 any MCV, ≥3 Hib, ≥3 hep B	17
Anderson et al 1997 (142)	Cross-sectional (household interviews)	688	Latino families with children aged 12-36 months residing in selected counties in Los Angeles	12-36 months	Los Angeles, USA (August-December 1992)	DTP, OPV (vaccine record)	3 DTP, 2 OPV by 12 months	12
Australian Institute of Family Studies (155)	Cohort (interview)	4779	Members of B-cohort Longitudinal Study of Australian Children who had given consent for their child's data to be linked	12, 24, 60 months	Australia (March 2003-February 2004)	DTP, IPV, Hib, Hep B, MMR (Australian Childhood Immunisation Register)	12 months – 3 DTP, 3 IPV, 2 Hib, 2 hep B 24 months – 3 DTP, 3 IPV, 3 Hib, 3 hep B, 1 MMR 60 months – 4 DTP, 4 IPV, 2 MMR	15
Bardenheier et al 2003 (109)	Cross-sectional (paper questionnaire)	648	Parents/legal guardians of kindergarten-enrolled children who resided in Butte County for at least 1 year and attended a public or private school in the county	4-5 year olds	USA (February-April 2000)	Hep A (Vaccination registry)	1 hep A	15
Bardenheier et al 2004 (168)	Case-control (telephone interview)	2315	Parents of US children aged 19-35 participating in 2000-2001 NIS. Cases (n=1016) – parents of children not UTD for ≥1 specified vaccine.	19-35 months	USA (January-December 2001)	MCV/MMR; DTP/DTaP; Hep B (physician-verified vaccination status)	≥4 DTP/DTaP, ≥3 polio, ≥1 MMR, ≥3 Hib, ≥3 hep B, ≥1 varicella	14

[2] Numbers refer to number of doses, if specified

			Control (n=1299) – parents of children UTD with all vaccines					
Bates et al 1994 (150)	Cohort (face-to-face interviews)	300	Parents of healthy full-term new-borns delivered at a large municipal teaching hospital	9-12 months	USA (Infants born April-September 1992; follow-up 9-12 months later)	DTP, polio (vaccination records)	3 months – 1 DTP and 1 polio by 90 days after birth 7 months - 3 DTP and 2 polio by 210 days after birth	15
Bedford 1990 (120)	Cross-sectional (postal questionnaire)	'Over 3000'	Parent of child aged 2 in selected health authorities	2 year olds	England and Wales (Not reported)	Measles and pertussis (not reported)	Vaccinated with measles or pertussis	3
Bennett & Smith 1992 (160)	Case-control (structured interview)	228	Parents of children in Mid-Glamorgan aged between 2-2.5 identified by Welsh Health Common Services Authority childcare database as being fully vaccinated (n=85); partially vaccinated (n=70); not vaccinated (n=73)	2-2.5 year olds	Wales (Not reported)	Pertussis (Welsh Health Common Services Authority childcare database)	Completed all pertussis vaccinations	12
Bigham et al 2006 (110)	Cross-sectional (telephone questionnaire)	487	Parents of children born between 1 January and 30 June 2001	15-24 months	British Columbia, Canada (October 2002-January 2003)	Hep B (self-report. Verified by information in Public Health Information System or immunisation provider)	1 Hep B	16
Bond et al 1999 (111)	Cross-sectional (Postal questionnaire)	1779	Parents of children attending council-run family day care or centre-based care for at least one day a week in metropolitan Melbourne	0-3 years	Melbourne, Australia (May-September 1997)	DTP, Hib, OPV, MMR (self-report. Verified by service provider where incomplete information given by parents)	First milestone: 3 DTP, 3 Hib, 3 OPV. Second milestone: 3 DTP, 3 Hib, 3 OPV, 1 MMR. Third milestone: 4 DTP, 4 Hib, 3 OPV, 1 MMR	16
Brenner et al 2001 (173)	Cohort (interviews)	370	Mothers of singleton births from 3 hospitals in the District of Columbia	7-12 months	USA (Infants born August 1995-September 1996; follow-up 7-12 months later)	DTP, polio, Hib (vaccination records)	3 months - 1 DTP, 1 polio, 1 Hib before 92 days 5 months - 2 DTP, 2 polio, 2 Hib before 152 days 7 months - 3 DTP, 2 polio, 2 Hib vaccines before 213 days	16
Bults et al 2011 (79)	Case-control (interviews, postal questionnaire)	3127	Parents of healthy children aged 6 months-5 years who did (n=1227) and did not (n=1900) accept the vaccine	6 months-5 years	Netherlands (vaccinated: 15-17 December 2009. Not vaccinated:18 June-27 July)	Influenza H1N1 (vaccinated recruited immediately after vaccination at clinic; decliners recruited in line with national register)	2 H1N1	13
Casiday et al 2005 (112)	Cross-sectional (postal questionnaire)	996	Parents of children registered with Primary Care Trust born between 1 October 2000 and 30 September 2002	1-3 years old	Lancashire, UK (May 2004)	MMR and single antigens (parent self-report)	Received MMR	15

			whose address could be determined using Child Health Information System					
Cassell et al 2006 (121)	Case-control (postal questionnaire)	452	Parents of children aged 15-24 months in Brighton and Hove primary care trust who are vaccinated for MMR (n=258)/not vaccinated (n=53)	15-24 months	Brighton and Hove, UK (March 2004)	MMR (Child Health Dataset)	Non-vaccinators – parents of children for whom no vaccinations were recorded on the Child Health Database. Compliant – reported choosing to have MMR before 15 months Non-compliant – those who delayed MMR vaccination, who did not vaccinate with MMR, who obtained single jabs, who remained undecided.	13
Clarke 1980 (161)	Cross-sectional (interviews)	53	Parents of families in a large urban practice in Leicester with children born in 1975 who had not completed primary immunisation course	3-4 years old	Leicester, UK (April-September 1978)	Diphtheria, tetanus, whooping cough, polio (Immunisation history recorded on computer)	Completed primary immunisation course of triple antigen (diphtheria, tetanus, whooping cough) and polio by 15 months	9
Cuninghame et al 1994 (122)	Cross-sectional (paper/telephone questionnaire)	93	Parents of Jewish orthodox children from three pre-specified practices aged under 2.5 years	0-2.5 years old	London, UK (June 1991-March 1992)	Diphtheria, pertussis, MMR (family doctor immunisation records)	6 months – 3 diphtheria, 3 pertussis 24 months – MMR	10
Dannetun et al 2005 (123)	Cross-sectional (telephone questionnaire)	199	Parents of children registered at Child Health Centres on 31st December 2002 in Östergötland who were born in 1998-2000 whose vaccination date was unknown	27-64 months	Östergötland, Sweden (January-February 2003)	MMR (parent self-report)	MMR vaccination	9
Dawar et al 2002 (124)	Cross sectional (phone interviews)	191	Parents of infants born in March 1999 in Vancouver/Richmond Health Board	8 months	Canada (November 1999)	Diphtheria, tetanus, pertussis, polio, Hib, hep B (Health Passport records held by parents or child's physician)	3 DPTP-Hib, 3 hep B	11
de Courval et al 2003 (125)	Cross-sectional (phone questionnaire)	178	Parents of children born between 30 April and 31 July 1999 identified from regional immunisation registry living in Quebec City area	14-17 months	Quebec City, Canada (July-October 2000)	Varicella (parent self-report)	Vaccinated for varicella	11
Dubé et al 2012 (113)	Cohort (phone questionnaire)	Phase 1 =413; phase 2=394	Future new parents expecting a child or parents of a healthy new-born aged 0-6 weeks in three Canadian cities (Vancouver, Quebec City, Halifax)	0-7 months	British Columbia, Quebec, Nova Scotia, Canada (2008-2009)	Rotavirus (parent self-report)	Received ≥1 rotavirus	12

Flynn & Ogden 2004 (126)	Cohort (postal questionnaire)	511	Parents of children born between 1 November 1997 and 31 January 1998 in Brighton and Hove area	2 years old	Brighton and Hove, UK (Not reported)	MMR (child health records)	MMR vaccination by age 2	14
Gellatly et al 2005 (127)	Cross-sectional (questionnaire)	110	Parents of children attending day-care nurseries in Edinburgh	1-59 months old	Edinburgh, UK (December 2003-May 2004)	MMR (parent self-report)	MMR vaccination	12
Gilkey et al (156)	Cross-sectional (telephone questionnaire)	9354	Parents of children aged 19-35 months participating in 2011 NIS	19-35 months	USA (Not reported)	MMR, varicella, seasonal influenza, tetanus-containing vaccine, polio, MCV, hep B, PCV (medical records)	36 months – ≥1 varicella, ≥1 seasonal influenza vaccine, ≥4 tetanus-containing vaccine, ≥1 MCV, ≥3 polio, ≥1 varicella, ≥3 Hep B, ≥4 PCV	14
Gore et al 1999 (114)	Cross-sectional (postal/telephone questionnaire)	316	Mothers in 18 rural counties who had children between the age group of 20-26 months as of May 31, 1994	20-26 months	West Virginia, USA (Not reported)	DTP, Hib, polio, MMR (parent self-report, where possible using immunisation records)	4 DTP, 4 Hib, 3 polio, 1 MMR	17
Gust et al 2004 (116)	Case-control (telephone interview)	1477	Parents/guardians of NIS participating children with adequate provider-reported immunisation data Case (n=463) – under-immunised (missing ≥2 high-profile vaccines) Controls (n=1015) – completely immunised	19-35 months	USA (January-December 2001)	DTP/DTaP, hep B, MCV (child vaccination records from vaccine provider)	≥2 DTP/DTaP, ≥2 hep B, ≥1 MCV	18
Gust et al 2008 (115)	Cross-sectional (face-to-face interviews)	3924	Parent or guardian of children aged 19-35 months	19-35 months	USA (April-December 2003 and April-December 2004)	DTP, polio, MMR, Hib, Hep B, varicella, PCV, influenza (parent self-report)	Vaccinated on time	13
Hughart et al 1999 (128)	Cross-sectional (telephone questionnaire)	466	Parents of children who made at least one visit to selected sites before age 2 years	24-30 months	Maryland, USA (Not reported)	DTP, MMR, OPV, Hib, hep B (medical record)	(1) Age-appropriate 1 DTP (2) Age-appropriate 3 DTP (3) Age-appropriate MMR, (4) 24 months – 4 DTP, 3 OPV, 1 MMR, 4 Hib (5) 24 months – 3 Hep B	12
Kaur 2011 (143)	Cross-sectional (postal questionnaire)	423	Parents of children born in Dundee in 1999 and 2000	3-4 years	Dundee, UK (2003)	MMR (parent self-report)	1 MMR vaccine	12
Kim 2004 (129)	Cross-sectional (face-to-face interview)	116	Korean immigrant mothers of children aged 2-5 years residing in inner-city area of Chicago	2-5 years	Chicago, USA (February-October 1998)	Hep B (Immunisation card/record, parent self-report)	3 hep B immunisation	14

Kim & Lee 2011 (171)	Cross-sectional (interview)	717	Parents of children aged 24-35 months living in Nonsan city, Korea	24-35 months	Korea (February-April 2005)	DTP, polio, MMR (vaccine record)	4 DTP, 3 polio, 1 MMR within 30 days of the recommended age	17
Lau et al 2013 (130)	Cross-sectional (Face-to-face interview)	401	Chinese parent of children aged 6-23 months who used one of 10 randomly selected Maternal and Child Health Centres	6-23 months	Hong Kong (May-June 2006)	Influenza (Parent self-report)	2 influenza	14
Lawrence et al 2003 (131)	Cross-sectional (telephone interview)	506	Parents of children born between 1 October and 31 December 1995 who were registered on ACIR on 4 May 2001	5 years old	Australia (July 2001)	MMR (Immunisation record or parental self-report)	2 MMR	12
Lewis et al 1988 (151)	Cohort (postal questionnaire)	2029	Parents of children born in Utah in June 1985	1 year old	Utah, USA (not reported)	Pertussis, DTP (parent self-report)	Vaccinated for pertussis	10
Maayan-Metzger et al 2005 (144)	Case-control (paper questionnaire)	204	Mothers of healthy term singleton babies who gave birth at a large tertiary hospital in Israel Cases (n=51) – unvaccinated for Hep B Controls (n=153) – vaccinated for Hep B	New born	Israel (January-September 2003)	Hep B (vaccine records)	Vaccinated for Hep B	12
MacDonald et al 2014 (117)	Case-control (postal questionnaire)	461	Parents/primary care givers of children who turned 2 between May 2008 and April 2009 Cases (n=130) – partially immunised Controls (n=331) – completely immunised	2 years old	Alberta, Canada (Not reported)	DTP, polio, Hib, MMR, varicella, men C, PCV. (Parent self-report)	4 DTP, 4 polio, 4 Hib, 1 MMR, 1 varicella, 3 men C, 4 PCV	17
Matsumura et al 2005 (152)	Cross-sectional (postal questionnaire)	5047	Parents of children who had an 18-month or a 36-month check-up at specified health centres	18 or 26 months old	Japan (November 2001-January 2002)	Measles (parent self-report)	Vaccinated for measles	11
Miller et al 1994 (153)	Case-control (telephone survey)	643	Parents of children who lived in selected counties in Colorado Cases (n=322) – had not received MMR by 2 years of age Controls (n=321) – had received MMR by 2 years of age	0-2 years	Colorado, USA (not reported)	MMR (immunisation records)	Vaccinated for MMR between 12-18 months	13
Morgan et al 1987 (132)	Cohort (interviews)	174	Parents of children who would reach 13 months during time allocated for interviewing parents in South East Thames Regional Health Authority	13-20 months	Maidstone, UK (not reported)	Measles (computer records)	Measles vaccination at 20 months	9
Muhsen et al 2012 (133)	Case-control (telephone survey)	270	Parent of children aged 2-5 belonging to ultraorthodox Jewish communities in Bnei Brak and Jerusalem	2-5 years Jerusalem; 2-	Israel (Not reported)	MMR, hep B, diptheria, tetanus, polio, pertussis, Hib (medical records,	1 MMR, 2 hep A, 3 hep B, 4 DT, 4 aP, 4 IPV, 4 Hib	11

			Cases (Bnei Brak=31; Jerusalem=28) – not adequately vaccinated for age Controls (Bnei Brak=77; Jerusalem=83) – adequately vaccinated for age	2.5 years Bnei Brak		immunisation card or parent self-report)	Cases received ≤20 doses (of 22 recommended doses) Controls received 21–22 doses	
Niederhauser et al 2001 (134)	Cross-sectional (telephone survey)	262	Parents of children who had a 24-month physical examination at Kaiser Permanente clinics in the state of Hawaii in 1998	2 years	Hawaii, USA (Not reported)	Varicella (parent self-report)	Varicella vaccination	12
Offutt-Powell et al 2014 (169)	Cross-sectional (paper questionnaire)	124	English-speaking parents or primary caregivers of children aged between 6 months and 5 years in selected day-care centres	6 months – 5 years	Texas, USA (not reported)	Influenza (parent self-report)	Received influenza vaccine	14
Opel et al 2013 (135)	Cohort (postal questionnaire)	437	English-speaking parents of children aged 2 months who were born from 10th July-10th December 2010 and part of Group Health Cooperative Seattle	2-19 months	Seattle, USA (questionnaire mailed October 2010)	DTP; inactivated poliovirus; MMR; Hib; hep B; varicella (Electronic immunisation record, immunisation registry)	Received all 16 doses by 19 months of age (does not report how many doses of each vaccine)	15
Pearce et al 2008 (96)	Cohort (face to face interviews)	14,578	Parents of children born in UK between September 2000 and January 2002 for whom information was available on MMR uptake at age 9 months	3 years	England, Scotland, Wales, Northern Ireland (Not reported)	MMR (Personal child health record)	Vaccinated with MMR	18
Pearce et al 2013 (518)		751	Same as above, and who were unimmunised for MMR at age 3	5 years			Unimmunised = received no MMR Partially caught-up = 1 MMR Fully caught-up = 2 MMR	
Peckham et al 1989 (136)	Cross-sectional (postal questionnaire)	3394	Parents of children born between 1 June 1985 and 31 December 1985	2 years old	England and Wales (Not reported)	Measles, pertussis (Parent self-report)	Vaccinated with measles and pertussis	12
Petrovic et al 2003 (137)	Case-control (postal questionnaire)	206	Parents of children born between 1 October and 31 December 1993, resident in North Wales on day of data extraction Case (n=54) – child had received all vaccines except second dose of MMR Control (n=152) – child had received all vaccines including second dose of MMR	4 years old	Wales (Questionnaires posted on 14-15 May 1998)	MMR second dose (Data provided by Health Solutions Wales)	Case = 1 MMR Control = 2 MMR	11

Prislin et al 1998 (145, 154)	Cross-sectional (in-person interviews)	4832	Parents of children in a household with a child aged 2-24 months in selected counties	2-24 months	Texas, USA (Not reported)	DTP, OPV, MMR (Vaccine records, parent-self report)	3 to 4 months – 1 DTP, 1 OPV 5 to 6 months – 2 DTP, 2 OPV 7 to 15 months – 3 DTP, 3 OPV 16 to 24 months – 4 DTP, 3 OPV, 1 MMR	15
		2368	Hispanic parents of children aged 3-24 months in selected counties	3-24 months				
Qutaiba B Al-lela et al 2014 (118)	Cross-sectional (interviews)	528	Parents of children younger than 2 years of age (born between 1 January 2003 and 31 June 2008)	0-2 years	Iraq (Not reported)	BCG vaccine, OPV, DTP, hep B virus, MMR vaccine, and the measles vaccine (Not reported)	24 months – 1 BCG, 5 OPV, 4 DTP, 3 hep B, 1 MMR	12
Richards & Sheridan 1999 (138)	Case-control (telephone survey)	191	Parents of children born in June and July 1994 in Brisbane North Regional Health Authority Group 1 (n=72) – fully vaccinated Group 2 (n=119) – not fully vaccinated	8 months	Brisbane, Australia (March 1995)	DTP, Hib, OPV (Parental report from vaccination record book, validated by database check)	3 DTP, 3 Hib, 3 OPV	11
Samad 2006 (162)	Cohort (face to face interviews)	18,488	Parents of children born in UK between September 2000 and January 2002	9 months	England, Scotland, Wales, Northern Ireland (Not reported)	Diphtheria, tetanus, polio, pertussis, Hib, men C (Mother's self-report and personal child health record)	3 diphtheria, 3 tetanus, 3 polio, 3 pertussis, 3 Hib, 3 men C	11
Schempf et al 2007 (146, 147)	Cohort (phone questionnaire)	4756	Families enrolled in Healthy Steps between September 1996 and November 1998	0-24 months	USA (September 1996-November 1998)	DTP, polio, MMR (vaccine records)	24 months – 4 DTP, 3 polio, 1 MMR	14
Smailbegovic et al 2003 (163)	Cross-sectional (postal questionnaire)	68	Parents of children resident in London Borough of Hackney born between 1 January 1999 and 15 February 1999 who had not completed the recommended course of immunisation	18 months	London, UK (not reported)	BCG, DT, pertussis, polio, Hib, men C, MMR (identified through population database, verified by parent self-report)	Completed recommended course of vaccines (includes universal BCG)	10
Smith et al 2015 (157)	Cross-sectional (telephone questionnaire)	12,259	Parents of children aged 19-35 months in 2010-2013 NIS	19-35 months	USA (2011-2013)	MCV (medical records)	≥1 MCV	12
Stahl et al 2013 (164)	Cross-sectional (online questionnaire)	3000	Mothers of children aged 0-35 months	0-35 months	France (September-November 2011)	Men C (parent self-report)	Vaccinated for men C	11
Stockwell et al 2011 (166)	Cross-sectional (interview)	392	Parents of children aged 2-36 months members of groups at selected community-based organisations	2-36 months	New York, USA (May 2007 - June 2008)	DTP/DTaP, polio vaccine, MCV, hep B, varicella (vaccine record)	4 DTP/DT/DTaP, 3 polio, 1 MCV, 3 hep B, 1 varicella within one month of due date	13

Strobino et al 1996 (172)	Cross-sectional (face-to-face interviews)	557	Parents of a birth cohort of children born between August 1988 and March 1989 to mothers who resided in 1 of 57 census tracts in Baltimore	0-24 months	Baltimore, USA (not reported)	DTP, OPV, MMR (vaccine records)	4 DTP, 3 OPV, 1 MMR by 24 months	15
Taylor et al 2002 (139)	Cross-sectional (questionnaire)	13,516	Parents of children aged 8-35 months enrolled at selected practitioners	8-35 months	USA (March 1998-January 2000)	DTaP, polio, Hib, hep B, MMR (medical records)	8 months – 3 DTP/DT/DTaP, 2 IPV/OPV, ≥2 Hib, ≥2 hep B 19 months – 4 DTP/DT/DTaP, 3 IPV/OPV, ≥3 Hib, 3 hep B, 1 MMR	15
Walsh et al 2015 (170)	Case-control (postal questionnaire)	308	Parents of children whose birthday was in July-September 2001 Cases (n=66) – Child received all routine immunisations except MMR by second birthday Controls (n=242) – Fully immunised	2.5-3 years	South Wales, UK (March-May 2002)	DTP, polio, Hib, MMR, men C (Parent self-report)	Received full primary course for DTP; polio; hib; ≥1 dose of MMR and men C	17
White & Lines 1996 (140, 159)	Cohort (postal questionnaire)	90	Parents of children aged 7 months in Adelaide	7 months	Adelaide, Australia (December 1991-September 1992)	Hep B (Parent self-report)	7 months – completion of the course of Hep B	6
Whiting et al 1990 (141)	Cross-sectional (telephone questionnaire)	72	Parents of children aged 24-60 months eligible for the Hib vaccine	24-60 months	Canada (not reported)	Hib (Parent self-report)	Vaccinated for Hib	11
Wolff & Madlon-Kay 2014 (165)	Case-control (paper questionnaire)	96	Somali (n=27) and non-Somali (n=69) parents of children aged ≤5 at a Clinic in Minneapolis	0-5 years	Minneapolis, USA (August 2012-February 2013)	MMR, hep B, varicella, DTaP, rotavirus, influenza (parent self-report)	Vaccinated for MMR, hep B, varicella, DTaP, rotavirus, influenza	12
Wu et al 2015 (148)	Cross-sectional (telephone interview)	540	Parents of Chinese children aged 24-59 months in Hong Kong	24-59 months	Hong Kong (March-June 2011)	Seasonal influenza (parent self-report)	Ever received influenza vaccination	13
Yawn et al 2000 (158)	Case-control study (postal questionnaire)	596	Parents of children born between 1 July 1992 and 30 June 1993 Case (n=70) – under-immunised Control (n=526) – fully immunised	2-3 years	Minneapolis, USA (not reported)	DTP, OPV/IPV, MMR (medical records)	20 months – 4 DTP, 3 OPV/IPV, 1 MMR	14
Zhao 2015 (149)	Cross-sectional (telephone questionnaire)	16, 919	Parents of children aged 19-35 months who had adequate provider data	19-35 months	USA (not reported)	DTaP (not reported)	18 months – 4 DTaP (dose 1 at 2 months; dose 2 at 4 months; dose 3 at 6 months)	9

ACIR – Australian Childhood Immunisation Register; aP – acellular pertussis; BCG – Bacille Calmette-Guérin; CDC – Centers for Disease Control; DPTP-Hib – vaccine for diphtheria, tetanus, pertussis, polio and haemophilus influenza B; DT – diphtheria and tetanus vaccine; DTP – whole-cell diphtheria and tetanus toxoids and pertussis vaccine; DTaP – diphtheria and tetanus toxoids with acellular pertussis vaccine; Hep A – hepatitis A; Hep B – hepatitis B; Hib – haemophilus influenza B; IPV – inactivated polio vaccine; MCV – measles containing vaccine; men C – meningitis C; MMR – measles, mumps and rubella vaccine; NIS – National Immunization Survey; OPV – oral poliovirus vaccine; PCV – pneumococcal conjugate vaccine; USA – United States of America; UK – United Kingdom; UTD – up-to-date vaccination status.

Appendix 2. Full table of results of factors affecting vaccine uptake in young children

Citation	Rate of uptake of vaccine	Psychological predictors of child vaccination considered, significant results in bold	Self-reported reasons for and for not vaccinating child
Alfredsson et al 2004 (119)	N/A	**No knowledge about vaccination before appointment. Parents' experiences from the vaccination procedure (dissatisfied with information provided by staff)**.	Reasons for not vaccinating: Vaccines are harmful; to strengthen child's immune system; measles, mumps and rubella are beneficial for child's development; parents have undergone diseases without harm; vaccination is unnecessary, other methods are better; measles, mumps and rubella are harmless Reasons for vaccinating: To protect child from measles, mumps and rubella; to prevent complications of measles, mumps, rubella; to strengthen child's immune system; parents have been vaccinated without complication; to protect the child when travelling abroad; the child has a chronic disease
Allred et al 2005 (167)	74%	**Vaccinations are safe.** Accept multiple vaccines at same time. Children who stay at home need same immunisations as those at school/day-care. Children can be vaccinated if they have a common cold. Acceptance of new vaccines. Child will get so ill from vaccination that they must see a doctor	
Anderson et al 1997 (142)	75%	**Acculturation**	
Australian Institute of Family Studies (155)	12 months – 93.5% (95% CI [92.7-94.3]) 24 months – 95.4% (95% CI [94.7-96.0]) 60 months – 81.4% (95% CI [80.1-82.6])	12 months. **Agreeing with vaccination.** Maternal psychological distress (moderate, symptomatic). Perceived time pressure. **Fewer stressful life events** (1 event; 2 events; **3+ events**). Hostile parenting (medium; high). Parental warmth (medium; high). 24 months. **Agreeing with vaccination.** Maternal psychological distress (moderate, symptomatic). Perceived time pressure. Fewer stressful life events (1 event; 2 events; 3+ events). Hostile parenting (medium; high). Parental warmth (medium; high). 60 months. **Agreeing with vaccination.** Maternal psychological distress (moderate, symptomatic). **Perceived time pressure**. Fewer stressful life events (1 event; 2 events; 3+ events). **Hostile parenting** (medium; **high)**. Parental warmth (medium, high).	
Bardenheier et al 2003 (109)	61.8% (398/648, 95%CI [56.9-66.8])	**Having heard of vaccine for hep A.** Thinking that hep A is major problem in Butte County. Thinking it is serious if child gets hep A. **Thinking child is likely to get hep A.** Thinking vaccine is safe. **Thinking kindergartners should be required to get hep A vaccine before school entry.**	
Bardenheier et al 2004 (168)	N/A	MCV/MMR. Concern about safety. **Refusal of any vaccine for child for reason other than illness.** Refused vaccine for child. Previous side-effect to an immunisation. Shots did not want for child but which were required by law. **If had a new baby, would want to get all immunisations.** Heard that vaccine causes side-effects. **Causes autism. Believing it causes autism.** Causes fever.	Reasons for not vaccinating: MCV/MMR. **Concerned about side-effects. Believed child received too many shots.** Unlikely that child would get disease. **Believed disease was not serious.** Wanted to postpone shot.

		Believing it causes fever. **Causes high fever. Believing it causes high fever.** Causes brain damage. DTP/DTaP. Concern about safety. **Refusal of any vaccine for child for reason other than illness**. Refused vaccine for child. **Previous side-effect to an immunisation**. Shots did not want for child but which were required by law. If had a new baby, would want to get all immunisations. Heard that vaccine causes side-effects. Causes autism. Believing it causes autism. Causes fever. Believing it causes fever. Causes high fever. Believing it causes high fever. Causes brain damage. Hep B. Concern about safety. **Refusal of any vaccine for child for reason other than illness**. Refused vaccine for child. Previous side-effect to an immunisation. **Shots did not want for child but which were required by law. If had a new baby, would want to get all immunisations.** Heard that vaccine causes side-effects. Causes autism. Causes fever. Believing it causes fever. Causes high fever. Believing it causes high fever. Causes brain damage. Believing it causes brain damage. Causes liver problems. Believing it causes liver problems.	DTP/DTaP. **Concerned about side-effects. Believed child received too many shots. Unlikely child would get disease. Believed disease was not serious.** Wanted to postpone shot. Hep B. **Concerned about side-effects. Believed child received too many shots. Unlikely child would get disease. Believed disease was not serious. Wanted to postpone the shot.**
Bates et al 1994 (150)	3 months. 67% (309/465). 7 months. 29% (135/464)	7 months. **Perceived logistical barriers. Perceived susceptibility to symptoms. Perceived benefit to prevent disease.**	
Bedford 1990 (120)	Not reported	**Perception of severity and infectivity of the disease. Perception of safety and efficacy of vaccines**	Reasons for not vaccinating: Measles (n=449). 21% advised by doctor/health visitor; 16% child unwell (no fever); 15% no appointment received; 10% had the illness; 6% did not attend, no further appointment received; 5% child had fever; 4% inconvenient time/place; 4% did not want it; 4% fear of vaccine; 16% other Pertussis (n=526). 43% advised by doctor/health visitor; 31% fear of the vaccine; 4% had the illness; 2% child had fever; 20% other
Bennett & Smith 1992 (160)	N/A	Pertussis vaccine. **Anxiety regarding permanent health problems as a result of vaccine. Likelihood of child developing illness if vaccinated. Likelihood of child developing illness if not vaccinated.** Perceived severity if contracted (without vaccination). **Perceived importance of vaccination.** MMR. **Anxiety regarding permanent health problems as a result of vaccine.** Measles. **Anxiety regarding permanent health problems as a result of vaccine.** Likelihood of child developing illness if vaccinated. Likelihood of child developing illness if not vaccinated. Perceived severity if contracted (without vaccination). **Perceived importance of disease vaccination.** Polio. Anxiety regarding permanent health problems as a result of vaccine. **Likelihood of child developing illness if vaccinated.** Likelihood of child developing illness if not vaccinated. Perceived severity if contracted (without vaccination). **Perceived importance of vaccination.** Diphtheria. Anxiety regarding permanent health problems as a result of vaccine. Likelihood of child developing illness if vaccinated. Likelihood of	

		child developing illness if not vaccinated. Perceived severity if contracted (without vaccination). **Perceived importance of vaccination.**	
Bigham et al 2006 (110)	88.9% (433/487; 95% CI [85.8%-91.4%]) 1 hep B	**Cues to action.** Perceived benefits. Perceived barriers. Perceived illness severity.	Reasons for not vaccinating (n=50): 24% concern about side-effects, 22% parental deferral to older age, 10% parental perception that their child was not at risk, 6% parent unaware of program, 38% other.
Bond et al 1999 (111)	84% (1494/1779; 95% CI [82%-86%]) completely immunised. 15% (272/1779; 95%CI [13%-17%] incompletely immunised 1% (13/1779; 95% CI [0.3%-1.1%] no immunisation	Complete immunisation. **Perceived vaccine safety.** Perceived vaccine efficacy First milestone. Perceived vaccine efficacy. **Perceived vaccine safety.** Pertussis (serious; susceptible). Meningitis (serious; susceptible). MMR booster uptake. **Perceived vaccine efficacy**. Perceived vaccine safety. **Measles** (serious; **susceptible)**. DTP/Hib booster uptake. Perceived vaccine efficacy. **Perceived vaccine safety.** Pertussis (serious; susceptible). Meningitis (serious; susceptible).	
Brenner et al 2001 (173)	3 months, 75%. 5 months, 54%. 7 months, 41%	3 months. Self-efficacy. Perceived social norms. **Fewer perceived barriers.** Previous experience. Social support. Internal locus of control. Perceived benefit of immunisation. 7 months. Self-efficacy. Perceived social norms. Perceived barriers. Previous experience. Social support. Internal locus of control. Perceived benefit of immunisation.	
Bults et al 2011 (79)	N/A	**Negative feelings after vaccination decision. No feelings of doubt about the vaccination decision. Social influence on vaccination decision. Less information seeking behaviour. Less advice sought from social network.**	Parental reasons for not vaccinating (n=1900): 50.6% fear of side-effects/harmful consequences; 45.8% just have a bad feeling about it; 38.7% vaccine was not thoroughly tested; 35.1% no trust in effectiveness of vaccine; 34.1% contradictory messages in media; 15.5% no trust in government; 14.5% my child is never sick; 10.2% principal convictions/belief in alternative medicine; 9.1% child was sick/had fever; 4.5% child has had Mexican influenza ; 3.9% other parents didn't vaccinate their child either; 3.3% underlying allergic symptoms; 2.8% practical barriers Parental reasons for vaccinating (n=1227): 43.4% don't want child to become sick; 9.9% Mexican influenza can be severe (hospitalisations/death); 5.5% the government advises it, so I do it; 5.5% if I don't do it, I will regret it; 2.7% pregnant woman/baby/vulnerable person in household; 2.1% child is very susceptible for infections like influenza ; 1.5% GP advises vaccine; 1.5% social environment (friends/family) accepted vaccine, so I do too; 1.4% trust in effectiveness of vaccine; 1.4% if it doesn't benefit, it won't harm either; 1.3% child has underlying disease; 1.1% child receives vaccines according to National Immunisation Program.
Casiday et al 2005 (112)	889 (89.3%) received MMR vaccine. 72 (7.2%) started a course of single-antigen vaccines,	**Perceived vaccine safety (scientific evidence shows no link between MMR and autism; cannot be proved with 100% certainty that MMR is safe; more time is needed to fully investigate effects of MMR vaccine; possible complications of MMR can be very serious for children), less appropriateness of separate vaccines as an alternative to MMR (separate**	

	but only 19 of these (26.4) had all 3 immunisations. 31 (3.1%) received neither MMR nor single antigens	**vaccines are safe for children; children receiving separate vaccines are at risk from time lag between vaccines; if separate vaccines were offered by NHS many people wouldn't show up for all three jabs), importance of immunisation (I have responsibility to have my child vaccinated for the protection of all children; people who don't vaccinate their kids put others at risk; my child is likely to get measles if s/he isn't vaccinated), trust in doctors and the government (doctors are too dismissive of what parents claim about the vaccine side-effects; if I have any concerns about MMR they are taken seriously by my doctor; parents should make health decisions for their own children rather than leaving it up to professionals,; government is too defensive about MMR; NHS does not recognise good intentions of parents who opt for single vaccines for child; government would stop MMR vaccine if there was evidence of serious risk; government does a good job of protecting us from risks to health)**	
Cassell et al 2006 (121)	N/A	**Later time when MMR became a concern. Less concern about family health in relation to MMR. Higher severity of measles**. **Higher perception of approval by others (health visitor; GP). Less feeling that reasons for choice are different from most people you know. Certainty that made correct vaccination decision. Wanting to know more about MMR to help you make decision.** Avoidance of talking to friends about MMR. **Not believing there is a chance of serious side effects from MMR if there is a weakness in that child. Each child's immune system is not different. Single vaccines are a larger concern than MMR. MMR is not too much in one go. It is not better to get immunity naturally. Inability to forgive oneself if child ever got measles. Ability to forgive oneself if child ever got autism or other side-effects. Not believing that most important thing is that parents have the choice. Believing it to be easier if you were just told, and it wasn't your decision.** Considering possible benefits to other children when deciding about MMR. **Right for health professionals to advise parents to have their child vaccinated for the benefit of other children. Government's responsibility to decide whether children should be vaccinated. Trusting the government over science. Fewer being suspicious of the influence of the pharmaceutical companies.**	
Clarke 1980 (161)	63% (116/182)		Reasons for not vaccinating (n=40): 65% adverse publicity; 25% advice from general practitioner/health visitor; 10% other reasons
Cuninghame et al 1994 (122)	3 Diphtheria, 86% (n=93). 3 Pertussis, 82% (n=93). MMR 79% (n=42)		Reasons for not vaccinating: Third diphtheria (n=4); 75% intend to have (delay), 25% minor acute illness. Third pertussis (n=8); 50% intend to have (delay), 25% minor acute illness, 25% side-effects concerns. MMR (n=9), 56% intend to have (delay), 22% minor acute illness, 11% side-effects concerns, 11% difficult access

Dannetun et al 2005 (123)	13.1% (26/199)		Reasons for not vaccinating: (n=70). 64% fear of side-effects; 50% better with natural immunity; 16% adjuvant; 9% small risk of disease
Dawar et al 2002 (124)	3 hep B, 73.8%; 2 hep B, 12.5%; 1 hep B, 0.5%; no hep B, 13.1%. 3 DPTP-Hib, 89.0%; 2 DPTP-Hib, 7.9%; 1 DPTP-Hib, 1.0%; no DPTP-Hib, 2.1%.		Reasons for not vaccinating (n=21): 52% lack of hep B program awareness on the part of the physician, 29% physicians or parents felt that the infants were not at risk of acquiring the hep B infection, 14% parents did not support the program either due to concern regarding possible adverse effects of vaccine, 5% due to adverse media publicity, 5% parent deferred the vaccination to the grade six program
de Courval et al 2003 (125)	33% (59/178)	**Vaccine safety. Vaccinator's recommendation.**	Reasons for not vaccinating (n not reported): 39% complications of disease not frequent enough; 32% complications of disease not serious enough; 39% vaccine too expensive; 35% weak vaccinator's recommendation
Dubé et al 2012 (113)	42% (165/394)	**Parental intention. Personal normative belief (parents' perceptions of moral correctness of having their child vaccinated). Having a doctor/nurse recommend the vaccine.** Vaccine administered orally rather than by injection. Difficulty in getting an appointment. **Cost of vaccine. Having vaccine given in fewer than three doses**. Having vaccine given in more than two doses. Having vaccine given at same time as other vaccines. Difficulty accessing doctor's office/public health immunisation clinics. **Less fear of side-effects. Smaller problem that vaccine will not protect against all diarrhoea. Vaccine given as part of universal immunisation program (free).**[3]	Reasons for not vaccinating (parents with vaccination intention, n=106): 51% child receiving enough vaccines; 48% vaccine not useful; 40% vaccine not included in free public vaccination program
Flynn & Ogden 2004 (126)	77.7% (397/511)	Encouragement from others, perceived risk of illness, guilt about consequences, prior experience of issues, **faith in the media, faith in the medical profession, belief that vaccination is unhealthy**	
Gellatly et al 2005 (127)	72.7% (80/110)	**Influence of current research findings as important. Finding information contained in leaflets and packs useful. Perceived importance of eradication of rubella. Perceived importance of risk of adverse reactions.** Government advice. Government pressure. Health professionals' advice. Health professional's opinion. Lack of information on single vaccines. Nature of long-term effects. Other allergic reactions. Perceived protection from illness in one dose.	
Gilkey et al (156)	85% completed all vaccines	**Vaccine confidence. Vaccine benefits. Vaccine harm.** Trust in healthcare provider.	
Gore et al 1999 (114)	65.2% fully immunised (206/316)	**Perceived clinical support. Positive attitude towards immunisation. Immunisation-related beliefs. Fewer general problems during immunisation.**	

[3] At the time of the study, the vaccine was recommended for all children in Canada, but was not included in the publicly funded vaccination programme, meaning that parents had to pay for the vaccine (approximately 150-220 US$)

Gust et al 2004 (116)	N/A	**Believing vaccines to be unsafe.** Believing vaccines to cause minor side-effects.	Reasons for not vaccinating Under vaccinated children. 57.2% side-effects; 33.7% too many shots Fully vaccinated children. 45.5%; 27.1% low perceived severity of illness
Gust et al 2008 (115)	Not reported	Vaccine is not effective. **Vaccine is not safe or may cause serious side-effects**	Reasons for not vaccinating (n=234) DTaP – 67.4% safety/side effect; 22.6% child was ill; 1.1% effectiveness; 0.5% do not know/refused; 8.4% other. Polio – 82.4% safety/side effect; 14.4% child was ill; 1.5% effectiveness; 1.7% other. MMR – 93.9% safety/side effect; 3.9% child was ill; 1.7% effectiveness; 0.5% other. Hib – 76.5% safety/side effect; 9.3% child was ill; 3.2% effectiveness; 11% other. Hep B – 62.2% safety/side effect; 26.9% effectiveness; 5.3% child was ill; 5.6% other. Varicella – 49.6% safety/side effect; 45.8% effectiveness; 2.4% child was ill; 0.9% cost; 1.3% other. PCV – 65.5% safety/side effect; 25.1% effectiveness; 8.0% child was ill; 0.9% missed/could not get appointment; 0.5% other. Influenza –53.3% effectiveness; 34.5% safety/side effect; 1.4% do not know/refused; 10.5% other.
Hughart et al 1999 (128)	(1) AA DTP1, 94.1%. (2) AA DTP3, 73.0%. (3) AA MMR, 67.6%. (4) UTD 4DTP, 3OPV, 1MMR, 4Hib, 70.6%. (5) AA 3 Hep B, 49.8%	Parental knowledge. Parental attitudes.	
Kaur 2011 (143)	94.3%	MMR1. **Fear (**measles; mumps; **rubella). Perceived severity of disease (**measles; mumps; **rubella). Vulnerability if not immunised (measles; mumps; rubella). Vulnerability if immunised (autism; IBD). Response efficacy (More dangerous to have MMR immunisation than to have measles; MMR immunisation weakens child's immune system; strong evidence of a link between MMR immunisation and autism; no strong evidence that MMR causes IBD). Internal self-efficacy (**Child's distress; **own anxiety)**. **Subjective norm: wanted to vaccinate (Partner; child's grandparents; friend;** GP; **health visitor). Followed advice (**partner; child's grandparents; **friend; GP; health visitor).** MMR2. Fear. **Severity of diseases.** Disease vulnerability if not immunised. **Autism/IBD vulnerability if immunised. Response efficacy: immunisation efficacy and attitudes. Response efficacy: safety evidence. Subjective norms.**	
Kim 2004 (129)	56% (n=65)	Difficulty remembering immunisation schedule. **Perceived severity of illness**. Perceived benefits of vaccine.	

Kim & Lee 2011 (171)	50.3% fully up-to-date. Age-appropriate immunization: 4 DTP, 51.7%; 3 polio, 88.0%; MMR, 87.9%.	Perceived susceptibility. Perceived benefit. Perceived severity. **Perceived barrier. Knowing when next shot will be.**	
Lau et al 2013 (130)	6.0%	Perceived susceptibility. Perceived severity. Perceived benefits of vaccination. **Perception of side-effects. Cue to action (recommendation from healthcare professional. Awareness of government's recommendation for vaccination.**	Reasons for not vaccinating (first dose; n not reported): 23.2% not necessary, 11.4% do not know/had not thought about it, 10.0% the baby is too young, 8.8% had not been recommended by healthcare professionals, 8.1% worry about side effects of influenza vaccine, 4.3% out of stock, 3.6% afraid of clashing with other injections, 3.1% vaccine not efficacious, 2.6% seldom go out, 2.4% did not know where to get influenza vaccine, 1.9% sick, 1.2% not living in HK, 0.9% busy, 0.7% did not want to take influenza vaccine, 0.7% vaccine taken more than 6 months previously was still efficacious, 0.7% cannot afford it, 0.7% allergic to influenza vaccine, 0.7% inadequate knowledge about influenza vaccine; 3% other. Reasons for not vaccinating (second dose; n not reported): 33.3% did not realise a follow-up dose was required, 16.7% out of stock, 16.7% child was sick, 33.3% other reasons
Lawrence et al 2003 (131)	MMR1, 91.7% MMR2 66.0%		Reasons for not vaccinating: (n=160): 28.8% knowledge of when second dose of MMR due, 18.1% illness/medical reasons, 16.3% forgot, 8.1% family logistical issues, 8.1% disagree with immunisation, 5.6% concerned about immunisation, 5.0% should have been given (at school) but no record or recall, 3.8% doctor did not offer MMR vaccination, 3.1% other, 3.1% unsure of reason
Lewis et al 1988 (151)	69% (n=1410) adequately immunised 26% (n=540) partially immunised 4% (n=79) not immunised	**Worry about vaccine.**	Reasons for vaccinating (adequately immunised; n=1410): 84.6% vaccine important, 10.6% physician recommended, 4.2% required by law, 0.6% required by day care. Reasons for vaccinating (partially immunised; n=530): 81.7% vaccine important, 10.3% physician recommended, 5.2% required by law, 0.7% required by day care.
Maayan-Metzger et al 2005 (144)	N/A	Multinomial logistic regression. Vaccinations given to babies in hospital are effective. **Vaccinations given to babies in the hospital are against dangerous diseases. Vaccinations approved by the Ministry of Health are not dangerous. Injections are very traumatic to the baby. If one had a choice, then home delivery is the best way to give birth. Parents have the right to determine the treatment given to their child.** Natural medicine is the best.	Reasons for not vaccinating (n not reported): 54.9% child is too young to be vaccinated, 19.6% doctors vaccinate without differentiation, 17.6% vaccines are dangerous, 13.7% it causes trauma to the baby, 9.8% mother was vaccinated. Reasons for vaccinating (n not reported): I trust the doctors, vaccines protect the baby.
MacDonald et al 2014 (117)	N/A	**Concern about vaccine safety. Lack of belief in disease susceptibility and severity, and vaccine effectiveness.** Distrust in medical professionals. Distrust in government. Bad immunisation experience with older child. Experience with side effect(s). Knew someone with vaccine-preventable disease. Positive experience with immunisation provider. Received adequate information on immunisation. Heard negative views about immunisations in the media.	

		Delayed immunisations in the past because too many needles at once. Considered not getting immunisation because of needle pain. **Getting immunisations was a hassle/difficult** (slightly difficult, somewhat difficult, **quite/very difficult**.	
Matsumura et al 2005 (152)	18 months, 73.2% 36 months, 88.9%	18-month olds. High knowledge, low concern (reference). **Low knowledge, low concern.** High knowledge, high concern. **Low knowledge, high concern.** 36-month olds. High knowledge, low concern (reference). **Low knowledge, low concern. High knowledge, high concern. Low knowledge, high concern.**	Reasons for not vaccinating. 18-month olds (n=698). 76.2% has not received it yet but will in near future, 32.5% had a cold at time of vaccination, 23.5% had to receive other vaccinations first, 22.2% wanted to receive it but missed the chance, 6.9% wasn't aware of/forgot about the vaccination schedule, 4.9% was sick at time of vaccination, 4.9% has already been infected with measles, 2.9% concern about adverse events of measles vaccination, 2.4% naturally acquired immunity seems more effective, 2.4% vaccination is no longer mandatory, 0.7% vaccination does not seem to be sufficiently effective, 5.4% other. 36-month olds (n=211). 46.9% has not received it yet but will in near future, 34.1% wanted to receive it but missed the chance,24.2% had a cold at time of vaccination, 11.8% has already been infected with measles,11.4% had to receive other vaccinations first, 9.5% wasn't aware of/forgot about the vaccination schedule, 9.5% concern about adverse events of measles vaccination, 6.6% vaccination is no longer mandatory, 4.7% naturally acquired immunity seems more effective,1.9% was sick at time of vaccination, 1.4% vaccination does not seem to be sufficiently effective, 3.3% other.
Miller et al 1994 (153)	N/A	Seriousness of illness. Susceptibility to illness. Efficacy of vaccine. Vaccine likely to be harmful. Worry about fever after vaccination. Believe that multiple vaccinations were unsafe. **Correct knowledge of age for MMR immunisation.**	
Morgan et al 1987 (132)	74% (129/174)		Reasons for not vaccinating (n=20): 35% decided against the immunization, with the main reasons being problems of fits in the family, the child's medical problems (generally an egg allergy or eczema) or because the child had already had measles, 65% 'delay' due to child having an illness and other worries, such as the harmful effects of the vaccine.
Muhsen et al 2012 (133)	N/A	**Religious belief against vaccines (Bnei Brak, Jerusalem. Low perceived risk of vaccine preventable diseases (Bnei Brak, Jerusalem). No trust in Ministry of Health vaccines (Bnei Brak**).	
Niederhauser et al 2001 (134)	71% vaccinated (187/262)	Awareness (knowledge, cues to action). **Assessment (perceptions, barriers, benefits). Decision-making (necessity of vaccine for child, thought about risks and benefits and decided vaccine was good, confident in vaccine preventing disease in child, importance of immunising child on time, sure my child needs the shot as the doctors and nurses told me it was important, not worried about how long the vaccine will protect my child from the disease, perceived severity of disease) - all together**	

Offutt-Powell et al 2014 (169)	65%	**Physician recommendation. Perceived threat of illness (high, moderate). Perceived risk of vaccine-related adverse events (high, moderate).**	
Opel et al 2013 (135)	66.1% fully vaccinated	**Lower score on PACV questionnaire**	
Pearce et al 2008 (96); Pearce et al 2013 (518)	88.6% (n=13,013)		Reasons for not vaccinating (n=1508). 74.4% conscious decision (of these 24.1% too scared/think the vaccine too dangerous, 18.6% do not want child to receive MMR, 14.1% fear over possible links with autism, 9.5% negative media attention), 12% medical issues, 3% practical issues, 10% other.
	23.6% (n=184) fully caught-up 16.1% (n=127) partially caught-up 60.3% (n=440) unvaccinated	**Reason for not having had MMR at age 3** (practical – reference), **(medical, other). Conscious decision.**	
Peckham et al 1989 (136)	Measles, 85% Pertussis, 84%	**Parents' attitude score: measles, pertussis.**	Reasons for not vaccinating Measles (n=449). 21% doctor/health visitor advised against vaccine; 16% child 'unwell' (no fever); 15% no appointment received; 10% had the disease; 6% did not attend (no further appointment received); 5% child had fever; 4% time/place inconvenient; 4% did not want it; 3% fear of vaccine; 16% other. Pertussis (n=526). 43% doctor/health visitor advised against vaccine; 31% fear of vaccine; 4% had the disease; 2% fever; 20% other
Petrovic et al 2003 (137)	N/A	**Influence from newspapers/television.** Perceived seriousness of illness. **Worry about MMR vaccine.**	Reasons for not vaccinating (n=33): 75.8% one dose of vaccine is enough, 63.6% worried about side-effects, 9.7% negative influence of a health visitor
Prislin et al 1998 (145, 154)	Not reported	**'Attitudes and perceived control significantly influenced up-to-date immunization: The more positive the attitudes and the stronger the sense of personal control, the better the immunization status'**	
	54%	**Less acculturation.**	
Qutaiba B Al-lela et al 2014 (118)	56.3% (n=286)	**Knowledge. Vaccination practice.**	
Richards & Sheridan 1999 (138)	N/A		Reasons for not vaccinating (n=16): 75% intended to finish the schedule/assumed they had completed it, 13% decided against vaccination after receiving one or more doses, 6% GP was seemingly unaware of the need for a third dose, 6% child had been judged too seriously ill for vaccination.
Samad 2006 (162)	95.6% (n=17,544) fully immunised 3.3% (n=712) partially immunised		Reasons for not vaccinating Partially immunised infants (n=697): 31.4% child unwell, 14.1% next appointment in near future, 5.4% parent unable to keep appointment, 5.3% parents not got round to it yet, 4.7% administrative error/difficulties, 4.5%

	1.1% (n=232) unimmunised		whooping cough vaccine excluded, 3.8% parental choice, 3.2% child unwell after last vaccination/allergic reaction, 2.9% did not want child to have all vaccines at once, 2.6% medical problems related to reaction to vaccination in family, 1.0% lack of supplies/ran out of vaccine, 0.1% staffing problems. Unimmunised infants (n=228): 9.9% associated health risks/concerns, 6.9% prefer to use homeopathic alternative/other method, 6.6% medical problems related to reaction to vaccination in family, 6.4% child is too young and prefer to wait until older, 3.2% administrative error/difficulties, 3.2% parents have not got round to it yet, 2.6% parental choice, 2.2% parent unable to keep appointment, 1.5% benefits do not outweigh the risks, 1.1% staffing problems, 0.5% parent dislikes needles/injections, 0.5% lack of supplies/ran out of vaccine.
Schempf et al 2007 (146, 147)	72.4%	Satisfaction with care.	
Smailbegovic et al 2003 (163)	57% (39/68) omitted MMR 49% (33/68) omitted men C 18% (12/68) omitted pertussis 15% (10/68) omitted BCG 6% received no vaccines		Reasons for not vaccinating (n=68): 68% vaccine safety; 27% time constraint; 19% lack of information
Smith et al 2015 (157)	Not reported	**Perceived necessity of vaccines to protect the health of children. Worry less about child's health after vaccinating. Perceived severity of measles as an illness that can hurt child. If don't vaccinate child, may catch illness and cause others to have illness too. Vaccines are effective. Children do not receive too many vaccines.** Influence of healthcare worker on vaccination decision. **Less influence of practitioner of complementary or alternative medicine on vaccination decision. Higher perceived encouragement from healthcare provider to vaccinate). Perception of enough time to discuss issues surrounding vaccination with doctor at appointments. Satisfaction with information about vaccination. Good relationship with child's healthcare provider. Perception that medical professionals in charge of vaccinations have child's best interest at heart.** Influence of school or day-care requirements on vaccination decision. **Vaccines are safe. Vaccines do not cause autism. Vaccines do not cause serious side-effects. Too many vaccines cannot overwhelm child's immune system. Vaccination should not be delayed if child has minor illness.**	
Stahl et al 2013 (164)	12-23 months, 32.3% 24-35 months, 57.3%	Consider vaccination useful. **Physician advice to vaccinate.**	
Stockwell et al 2011 (166)	Not reported	Ever having a child under-immunised. **Negative previous immunisation experience.**	

Strobino et al 1996 (172)	283 (54%) UTD. 71% (374) age appropriate DTP1, 35% (186) age appropriate DTP3, 53% (276) age appropriate MMR	DTP1 age-appropriate immunisation. Not important if child misses a shot. Less than sure can complete steps to get child immunized. Bringing other children to clinic is a hassle. It is safe to get more than one shot at a time. Keeping shots up-to-date is not the norm. Total time at last visit was long (≥90 min). Shots are effective. DTP3 age-appropriate immunisation. **Not important if child misses a shot.** Less than sure can complete steps to get child immunized. **Bringing other children to clinic is a hassle.** It is safe to get more than one shot at a time. Keeping shots up-to-date is not the norm. Total time at last visit was long (≥90 min). Shots are effective. MMR age-appropriate immunisation. **Not important if child misses a shot.** Less than sure can complete steps to get child immunized. Bringing other children to clinic is a hassle. It is safe to get more than one shot at a time. Keeping shots up-to-date is not the norm. Total time at last visit was long (≥90 min). Shots are effective. UTD. **Not important if child misses a shot.** Less than sure can complete steps to get child immunized. Bringing other children to clinic is a hassle. It is safe to get more than one shot at a time. **Keeping shots up-to-date is not the norm.** Total time at last visit was long (≥90 min). **Shots are effective.**	
Taylor et al 2002 (139)	79.0% (10,684/13,520) 19+ months, 66.3%	8 months. **Confusing vaccination schedule. Expense of vaccines. Inconvenience of vaccination process. Child often too ill to receive vaccinations. Religious objections. Any significant barrier.**	
Walsh et al 2015 (170)	N/A	**Influence (newspapers, television, internet, vaccine pressure groups). More influenced by a health visitor**. Measles is a mild disease. MMR is ineffective. **Vaccines are protective. MMR does not cause serious diseases**. **Side-effects of MMR are seriously researched. There is not a conspiracy.** Infectious diseases would disappear without vaccines. **Infections are not good for the immune system. The second dose is essential. Three-in-one is not harmful. MMR has been thoroughly researched.**	
White & Lines 1996 (140, 159)	70.1%	Knowledge. **Number of barriers.**	
Whiting et al 1990 (141)	51% (37/72)		Reasons for not vaccinating (n=35): 80% other (lack of prior knowledge, physician advice, lack of time), 29% physician advice, 25% lack of prior knowledge, 20% possible side effects, 14% lack of scientific data, 11% ill child, 7% lack of time, 7% (2/35) lack of vaccine, 7% other
Wolff & Madlon-Kay 2014 (165)	22.2% Somali parents refused vaccine. 5.8% non-Somali parents refused vaccine.		Reasons for not vaccinating (n not reported): 57.1% heard problems with the vaccine, 42.9% personally knowing someone who had suffered adverse effects to the vaccine. Reasons for vaccinating (n not reported). Trust healthcare provider's judgement, concern over child becoming ill, disease spreading in community.

Wu et al 2015 (148)	58.9% 42.4% had two or more doses	**Perceived susceptibility. Number of items responses reflecting perceived benefits (1-3 items; 4+ items). Number of items responses reflecting perceived barriers (**1-3 items; **4+ items). Number of items responses reflecting cues to action (1-3 items; 4-5 items). Subjective norm). Fear during H1N1 pandemic.**
Yawn et al 2000 (158)	N/A	**Problems with transport. Child had been ill. Did not know when next vaccine needed. Hard to remember appointment. Afraid child would have reaction to injection.** Do not like the HCW. Doctor advised child not to have the injection. Clinic location not convenient. Injection too expensive. Did not want to put child through pain of injection. Did not want child to have more than one injection at a time.
Zhao 2015 (149)	85.3%	**Confidence in value of vaccines. Confidence in efficacy of vaccines. Confidence in safety of vaccines. Parents have good relationship with providers.**

BCG – Bacille Calmette-Guérin; DTP – whole-cell diphtheria and tetanus toxoids and pertussis vaccine; DTaP – diphtheria and tetanus toxoids with acellular pertussis vaccine; GP – general practitioner; Hep A – hepatitis A; Hep B – hepatitis B; Hib – haemophilus influenza B; HK – Hong Kong; IBD – irritable bowel disease; MCV – measles containing vaccine; men C – meningitis C; MMR – measles, mumps and rubella vaccine; N/A – not applicable; NHS – national health service; OPV – oral poliovirus vaccine; PACV – Parent Attitudes About Childhood Vaccines survey; PCV – pneumococcal conjugate vaccine; UTD – up-to-date vaccination status.

Appendix 3. Methods of articles included in systematic review of factors affecting parental perception of symptoms in one's child

	Study design (method)	Number of participants (child age)	Inclusion criteria	Risk of bias
Akbarzadeh et al 2018 (359)	Cross-sectional (questionnaire and interview)	212 (7-16 years. Mean age 9.83 years)	Parents of children with a diagnosis of chronic or recurrent headache in Tehran, Iran	12
Aromaa et al 1998 (355)	Case-control, as part of wider prospective cohort study (questionnaire)	968 (6 years)	Parents of children in Finnish Family Competence Study with (n=144) and without headache (n=764) in preceding 6 months	9
Baldin et al 2012 (360)	Cross-sectional (questionnaire)	9679 (7-15 years. Mean 10.83 years)	Parents of school children in all public and private schools in Reykjavik, Iceland school district	8
Borge & Nordhagen 1995 (356)	Prospective cohort (interview)	139 (10 years)	Parents of children in a rural birth cohort in Norway	7
Cerutti et al 2017 (345)	Cross-sectional (paper questionnaire, delivered to parents by children)	356 (8-15 years)	Parents of children aged 8-15 who were not undergoing pharmacological or psychological therapy, or had an existing diagnosed infection/other medical illness, in Italy	9
Correia & Linhares 2013 (361)	Case-control (face-to-face interview)	75 (3-5 years)	Mothers of preschool children who were registered in the Family Health Program in South-East Brazil	11
Domenech-Llaberia et al 2004 (246)	Cross-sectional (postal questionnaires)	807 (3-6 years)	Parents of children attending pre-school public and private nurseries in Spain	8
Fabbri et al 2012 (343)	Prospective cohort (questionnaire)	1674 (7-11 years)	Parents of children born in two areas of Brazil	12
Fearon & Hotopf 2001 (362)	Prospective cohort (interview)	9841 (7-11 years)	Parents of children born in Great Britain from 3-9 March 1958	10
Fryer et al 2017 (374)	Cross-sectional (questionnaire)	8463 (11 years)	Parents of children in the fifth wave of the UK Millennium Cohort Study	13
Gassmann et al 2012 (363)	Prospective cohort (questionnaire)	3984 (7-15 years. Mean age 11.3)	Parents of children in the Children, Adolescents & Headache Study ('KiJuKo') in Germany	8
Giacobo et al 2012 (346)	Cross-sectional (paper questionnaire)	319 (3-6 years)	Parents of children enrolled in specific schools in Barcelona, Spain	9

Gibb 2014 (347)	Cross-sectional (questionnaire and interview)	1368 (7-11 years)	Parents of children at selected schools in England	10
Giray et al 2018 (364)	Cross-sectional (questionnaire)	85 (4-12 years. Mean age 7.1±2.5 years)	Mothers of children with cerebral palsy attending an outpatient clinic between February and April 2016, in Turkey	12
Grunau et al 1994a (348)	Case-control (paper questionnaire at 18-month visit)	195 (18 months)	Case 1, extremely low birth weight: parents of children who weighed less than 801g (n=49). Case 2, extremely low birth weight: parents of children who weighed 801-1000g (n=75). Control: parents of pre-term children who weighed 1500-2499g (n=42). Control: parents of full-birth-weight children, >2499g (n=29)	6
Grunau et al 1994b (349)	Prospective case-control (paper questionnaire at multiple visits, observation of mother-child interaction at 3 year visit)	72 (4.5 years)	Case: extremely low birth weight: parents of children who weighed 1000g or less Control: parents of full-term children with birthweight >2500g	5
Henriksen & Thuen 2015 (365)	Prospective cohort (questionnaire)	8788 (6-11 months)	Mothers of children enrolled in the Norwegian Mother and Child Cohort Study	9
Kilgallen & Gibney 1996 (357)	Cross-sectional (interview-assisted questionnaire)	600 (0-48 months)	Parents of children attending an antenatal or postnatal clinic in two Dublin, Ireland hospitals; or attending some immunisation clinics	7
Kohler et al 2017 (366)	Cross-sectional (postal questionnaire)	6728 (4 years)	Parents of children in Skåne (Scania), Sweden	13
Link & Fortier 2016 (367)	Cross-sectional (questionnaire, either at home or at scheduled appointment)	353 (0-18 years. Mean age 10.6 years)	Parents of English and Spanish speaking children undergoing treatment and attending routine visit at Hyundai Cancer Institute at Children's Hospital of Orange County, USA between November 2009 and October 2011	12
Litcher et al 2001 (350)	Cross-sectional (home interviews)	600 (10-12 years)	Parents of children in Kyiv, Ukraine	10
Morris 2006 (344)	Cross-sectional (postal questionnaire)	5474 (7-14 years. Mean age 10.3 years)	Parents of children in the Children, Adolescents & Headache Study in Germany	13
Pitrou et al 2010 (368)	Cross-sectional (questionnaire)	1308 (6-11 years)	Parents of children in selected primary schools in France	12

Poder et al 2010 (369)	Prospective cohort (telephone questionnaire)	214 (0-18 years)	Parents of children recently diagnosed with cancer who were scheduled for chemotherapy or radiotherapy in certain paediatric oncology centres in Sweden	11
Ramchandani et al 2005 (371); Ramchandani et al 2006 (372); Ramchandani et al 2007 (370)	Prospective cohort (questionnaire)	30 months, n=10,205. 42 months, n=9845. 81 months, n=8272. 7 years	Mothers of children resident in Avon, England, with an expected date of delivery between April 1st 1991, and December 31st 1992	14
Rocha et al 2003 (351)	Cross-sectional (postal questionnaire, and inoculation appointment)	163 (56-68 months. Mean age 62 months)	Mothers of kindergarten children in Canada	6
Soltis & Shelestak 2011 (352)	Prospective cohort (paper questionnaire)	44 (1 month – 9 years. Median age 27 months)	Parents of children scheduled for voiding Cystourethrogram in Ohio, USA	7
Srivastava et al 2001 (353)	Prospective cohort (paper questionnaire)	25 (1 week – 6.5 years. Median age 0.62)	Parents of children referred for a micturating cystourethrogram procedure	6
Stevenson et al 1988 (354)	Cross-sectional (face-to-face interview)	189 (2.5-3.5 years)	Parents of children aged 2.5 to 3.5 years in the UK	3
Strine et al 2006 (342)	Cross-sectional (interview)	9399 (4-17 years)	Parents of children in the 2003 National Health Interview Survey Sample Child Core in the USA	16
Wolff et al 2010 (373)	Prospective cohort (postal questionnaire)	5171 (Questionnaires sent at age 18 months. Mean age 18.4 months)	Parents of children in Generation R Study in Rotterdam, Netherlands	14
Zuckerman et al 1987 (358)	Prospective cohort (face-to-face interviews)	308 (0-3 years, T1 at 8 months, T2 at 3 years)	Parents of children in a postnatal mothers' group held in London, UK	8

Appendix 4. Full table of results of factors associated with parental report of symptoms. Unless stated, predictors are reported by the same person reporting symptoms and relate to child factors.

	Symptoms perceived	Measure of symptoms	Predictors of symptom perception
Akbarzadeh et al 2018 (359)	Pain severity of headache	Numeric pain rating scale	Mothers' ratings of child pain: **mother catastrophising about pain, anxiety,** depression Fathers' ratings of child pain: father catastrophising about pain, **anxiety,** depression
Aromaa et al 1998 (355)	Disturbing headache	'Has your child had headache disturbing his/her daily activities during the last 6 months? Has your child had headache disturbing his/her daily activities at some time in his/her life (before the last 6 months)?' Answered yes to both questions to be case	**Maternal perception of child poor health (9 months), high sociability (5 years), behavioural problems (5 years)**
Baldin et al 2012 (360)	Recurrent symptoms	'Has the child had any of the following symptoms?' Has the child 'ever complained of recurrent abdominal pain?'	Migraine: **fearful or anxious** Recurrent abdominal pain: **being fearful or anxious** Recurrent body pain: **being fearful or anxious** Recurrent stomach bugs with vomiting: **being fearful or anxious** Recurrent vomiting without cause: **being fearful or anxious** Recurrent nosebleeds: **being fearful or anxious** Recurrent dizzy spells: **being fearful or anxious** Recurrent concussions from minor head injuries: being fearful or anxious Recurrent fainting spells: being fearful or anxious Recurrent visual disturbances: **being fearful or anxious** Recurrent spells rapid/irregular heartbeat: **being fearful or anxious** Recurrent chest pains: **being fearful or anxious**

			Recurrent episodes of unexplained fever (>38): **being fearful or anxious** Recurrent episodes of diarrhoea: **being fearful or anxious** Recurrent wry neck (torticollis): **being fearful or anxious** Moving sickness: **being fearful or anxious** Tender hair: **being fearful or anxious** Other recurrent symptoms: **being fearful or anxious**
Borge & Nordhagen 1995 (356)	Headache, stomach ache	'Occurrence versus non-occurrence,' frequency of complaint	Headache and stomach ache co-occurrence: emotional problems (10 years), **maternal emotional support**, **behaviour problems (4 years)**, **emotional problems (4 years)**
Cerutti et al 2017 (345)	Somatic symptoms	Short version of the Children's Somatization Inventory – Parent version	**Difficulty in physical and psychological functioning. Alexithymia** (**difficulty identifying feelings** (*child-reported*), difficulty describing feelings *(child-reported)*, externally-oriented thinking *(child-reported)*)
Correia & Linhares 2013 (361)	Headache	'Duration and characteristics of [headache] episodes over the last six months'	Adverse life events, extraversion (activity level, high-intensity pleasure, impulsivity, shyness), negative affect (anger/frustration, **discomfort,** fear, sadness, soothability), effortful control (attention focusing, inhibitory control, low-intensity pleasure, perceptual sensitivity), approach/positive anticipation, smiling/laughter, maternal stress
Domenech-Llaberia et al 2004 (246)	Presence and frequency of physical symptoms (stomach aches, headaches, leg pains, tiredness, dizziness)	'Questionnaire… inquired about the presence and frequency once, two or three times, over three times) of four somatic complaints in the 2 weeks prior to assessment'	Frequently complaining children (4 or more complaints vs no complaints): **ADHD inattentive, generalised anxiety disorder, adjustment disorder, number of stressful life events, maternal mental distress**
Fabbri et al 2012 (343)	Headache	≥2 episodes of headache in the past two weeks, without any associated organic symptoms	Ribeirão Preto: **strengths and difficulties** São Luís: **strengths and difficulties**
Fearon & Hotopf (362)	Headache	'Does your child suffer from frequent headache or migraine?'	Headache: **moderate or severe depression (age 7), mental illness in family member (age 7)** Recurrent headache: **moderate or severe depression (age 7), mental illness in family member (age 7)**

Fryer et al 2017 (374)	Frequent complaints of pain	Parents asked whether child 'often complains of headaches, stomach-aches or sickness'	**Maternal distressed mental health (at child 3 years), child strengths and difficulties at 5 years**
Gassmann et al 2012 (363)	Recurrent headache	Headache frequency	Boys: reaction to failure, dysfunctional stress coping, anger out, anxiousness/depressiveness, aggressive behaviour Girls: age, reaction to failure, **dysfunctional stress coping**, anger out, anxiousness/depressiveness, hyperactivity
Giacobo et al 2012 (346)	Presence and frequency of physical symptoms (stomach ache, headache, fatigue, dizziness, and other complaints)	Qüestionari Pels Pares (Questionnaire for Parents)	Frequent somatisation: **any anxiety symptoms, separation anxiety, social phobia,** psychiatric symptoms (ADHD, generalised anxiety, specific phobia, depression, dysthymia, conduct disorder, oppositional defiant disorder), aggressiveness towards peers, severe mood dysregulation Stomach ache: **any anxiety symptoms, separation anxiety, social phobia** Leg pain: **any anxiety symptoms, separation anxiety,** social phobia Head ache: any anxiety symptoms, **separation anxiety,** social phobia Fatigue: any anxiety symptoms, separation anxiety, **social phobia**
Gibb 2014 (347)	Somatic symptoms	Children's Somatization Inventory – Parent version	**Anxiety, frequency of stressors (*child-reported*),** communication scale (*child-reported*: total communication, communication with primary caregiver, open communication, **inhibited confiding***, confiding of distress, **caregiver responsiveness***, sharing of news, confiding in friends) * When control for child-reported anxiety, but not parent-reported anxiety, association becomes non-significant
Giray et al 2018 (364)	Pain	Non-communicating children's pain checklist-revised	**Quality of life,** parental depression
Grunau et al 1994a (348)	Pain sensitivity	'Child is very sensitive to pain of bumps or cuts or other common hurts.' Likert scale of 1 to 5 from 'not characteristic' to 'very characteristic.'	Differences between groups: **Temperament** (not in children <801g), parenting style (organisation, variety, responsivity, acceptance, involvement)

Grunau et al 1994b (349)	Somatisation (at 4.5 year visit)	30 items which include questions about occurrence of stomach aches, headaches, leg pains among others	Somatisation in extremely low birth weight group (correlations): mother interaction (gratification, **sensitivity,** affect), child interaction (gratification, responsiveness, affect), **parenting style** (acceptance, **involvement**, responsivity), child's temperament (shyness, emotionality, sociability, activity), avoidance of touch, **family conflict** Somatisation in full-term group (correlations): mother interaction (gratification, sensitivity, affect), child interaction (gratification, **responsiveness**, affect), parenting style (acceptance, involvement, responsivity), child's temperament (shyness, **emotionality**, sociability, activity), avoidance of touch, **family conflict** Somatisation (stepwise multiple regression): **family conflict**
Henriksen & Thuen 2015 (365)	Infectious disease: common cold, throat infection, pneumonia/respiratory syncytial virus/bronchitis, diarrhoea/gastric influenza , ear infection, pseudocroup, urinary tract infection, conjunctivitis	Mothers marked a checklist which asked 'whether their children had or had not experienced a disease'	<6 months old, common cold: **maternal stressful life events, maternal relationship dissatisfaction** <6 months old, throat infection: **maternal stressful life events, maternal relationship dissatisfaction** <6 months old, pneumonia/respiratory syncytial virus/bronchitis: maternal stressful life events, **maternal relationship dissatisfaction** <6 months old, diarrhoea/gastric influenza: **maternal stressful life events, maternal relationship dissatisfaction** <6 months old, ear infection: **maternal stressful life events, maternal relationship dissatisfaction** <6 months old, pseudocroup: **maternal stressful life events, maternal relationship dissatisfaction** <6 months old, urinary tract infection: **maternal stressful life events, maternal relationship dissatisfaction** <6 months old, conjunctivitis: **maternal stressful life events, maternal relationship dissatisfaction** 6-11 months old, common cold: **maternal stressful life events, maternal relationship dissatisfaction** 6-11 months old, throat infection: **maternal stressful life events, maternal relationship dissatisfaction**

			6-11 months old, pneumonia/respiratory syncytial virus/bronchitis: **maternal stressful life events, maternal relationship dissatisfaction** 6-11 months old, diarrhoea/gastric influenza: **maternal stressful life events, maternal relationship dissatisfaction** 6-11 months old, ear infection: **maternal stressful life events, maternal relationship dissatisfaction** 6-11 months old, pseudocroup: **maternal stressful life events, maternal relationship dissatisfaction** 6-11 months old, urinary tract infection: maternal stressful life events, maternal relationship dissatisfaction 6-11 months old, conjunctivitis: **maternal stressful life events, maternal relationship dissatisfaction**
Kilgallen & Gibney 1996 (357)	Food allergy	'presence or absence of perceived food allergy'	**Maternal perception that general prevalence of food allergy is common**
Kohler et al 2017 (366)	Recurrent abdominal pain	'How often has the child had abdominal pain during the past 6 months?' Outcome dichotomised: 'Yes' if answer 'practically every day' or 'more than once a week.' 'No' if more rarely than once a week	Child factors: **violence in the family**, serious life event Maternal factors: **worries about economy**, low emotional support, **everyday stress** Paternal factors: **worries about economy, low emotional support,** everyday stress
Link & Fortier 2016 (367)	Pain severity. Frequency of chronic pain	Pain severity: 0-10 numeric rating scale. Frequency of chronic pain in past 3 months: six-point Likert scale, 'every day' to 'less than once per month'	Pain severity: Parent trait anxiety Pain frequency: **Parent trait anxiety**
Litcher et al 2001 (350)	Somatic symptoms	Children's Somatization Inventory – Parent version, amended	**Child behaviour somatisation, child behaviour depression/anxiety, depression** *(child-reported)***, anxiety** *(child-reported)***,** perceived competence *(child-reported)*, self-worth *(child-reported)*

Morris 2006 (344)	Weekly headache versus good health	Experienced headache in last six months. Frequency 'at least once a week.' Specify absolute number of headaches in certain time span	**Anger-out mode of expression**, anxiety/depression, sleep disturbance, index of life events
Pitrou et al 2010 (368)	Frequent headaches	'Since his/her birth, did your child have frequent headaches, including migraines?'	Parenting style (**punitive behaviours, inverse association;** caring behaviours, overprotective behaviours), **emotional problems,** conduct disorder, peer relationship difficulties, hyperactivity-inattention, **abnormal total difficulties on Strengths and Difficulties questionnaire, general anxiety disorder** *(child-reported)***,** separation anxiety disorder *(child-reported)*, specific phobia *(child-reported)*, major depressive disorder *(child-reported)*, ADHD *(child-reported)*, oppositional defiant disorder *(child-reported)*, conduct disorder *(child-reported)*
Poder et al 2010 (369)	Symptom presence, frequency, intensity and distress	Modified version of the Memorial Symptom Assessment Scale 10-18 (Physical symptom scale)	**Parental PTSD**
Ramchandani et al 2005 (371); Ramchandani et al 2006 (372); Ramchandani et al 2007 (370)	Abdominal pain	'Have there been times when he/she seems to have had a pain in his stomach in the past 12 months?' Yes/No. 'How many separate times has this happened in the past 12 months?' If ≥5 a year, in recurrent abdominal pain group	30 months: **maternal anxiety, maternal depression,** partner anxiety, partner depression 42 months: **behavioural and emotional problems (hyperactivity, emotional, conduct, prosocial, total difficulties)** 81 months: **strengths and difficulties (hyperactivity**, **emotional, conduct, peer problems,** prosocial, **total difficulties, adjusted emotional), activity (temperament), rhythmicity of eating and sleeping (temperament), maternal anxiety** *(mother-reported)***, paternal anxiety** *(father-reported)* 7 years: hyperactivity score, emotional score, peer problems, **maternal anxiety**, paternal anxiety
Rocha et al 2003 (351)	Somatic symptoms	Children's Somatization Inventory – Parent version	Behavioural style (**adjustment**, sensitivity, activity/persistence), illness behaviour encouragement, **child's facial responses to pain reactivity** *(trained coder rating)*, maternal response to child's inoculation *(trained coder rating)*

Soltis & Shelestak 2011 (352)	Pain	Visual analogue scale – 10cm long with 100 points, 'perception of pain'	Parental anticipatory anxiety, **parental high experienced anxiety**
Srivastava et al 2001 (353)	Pain	Visual analogue scale – 10cm long with 100 points, 'perception of pain'	Parental anticipatory anxiety, **parental high experienced anxiety**
Stevenson et al 1988 (354)	Recurring stomach aches	Child experiencing a stomach ache during the preceding 4 weeks and during any time prior to this	**Behaviour (temper tantrums,** dependency, **fears**), maternal perception of inadequate social support, maternal depression, maternal irritability with child
Strine et al 2006 (342)	Frequent or severe headaches	'During the past 12 months, has [child's name] had frequent or severe headaches, including migraines?'	**Emotional symptoms (worried, unhappy, nervous, scared, total emotional domain), conduct problem (loses temper, less well behaved, fights/bullies, lies/cheats,** steals, **total conduct problem domain), hyperactivity-inattention (restless, fidgety, poor concentration, less reflective, less attentive, total hyperactivity-inattention domain), peer problems (plays alone,** has good friend, popular, **bullied, relates better to adults than peers, total peer problems domain), total high difficulties prevalence**
Wolff et al 2010 (373)	Presence and frequency of somatic complaints	Child Behaviour Checklist	Temperament (activity level, distress to limitations, **fear**, duration of orienting, **falling reactivity**, sadness), maternal prenatal symptoms (depression, **anxiety**), maternal symptoms at 2 months (depression, **anxiety**), **parenting stress**
Zuckerman et al 1987 (358)	Recurring headaches and stomach aches	At 3-year interview, if parent stated that child had experienced a headache or stomach ache in the last 4 weeks and at any time before this	Headache: **Behaviour problems (dependent, fears),** maternal concerns about child's appetite, **maternal depression,** maternal perceived inadequate support Stomach ache: **Behaviour problems (dependent**, fears**)**, maternal concerns about child appetite, **maternal depression**, maternal perceived inadequate support

Abbreviations: ADHD = attention-deficit hyperactivity disorder, PTSD = post-traumatic stress disorder

Appendix 5. Cross-sectional survey

- Survey data have been weighted by age, gender, region and working status to reflect the profile of parents/guardians of 2-7 year-old children in England[4].
- Results are based on all respondents (n=1,001) unless otherwise stated. Bases specified are unweighted.
- Where percentages do not sum to 100, this may be due to respondents being able to select multiple responses, computer rounding or the exclusion of 'don't know'/ not stated.
- An asterisk (*) represents a value of less than half or one percent, but greater than zero.

Q1. Please type in your age:

	%
18-24	4
25-44	37
45-54	46
55-64	13
65-74	1

Q2. Which gender do you identify yourself with?

	%
Male	43
Female	57

Q3. In which of the following regions do you live?

	%
North East	5
North West	12
Yorkshire and Humberside	12
West Midlands	11
East Midlands	9
East of England	10
South West	11
South East	17
London	14

[4] Please note that because data on parents of children aged 2-7 specifically was not available, data from the National Readership Survey (NRS) on parents of children aged 2-10, was used as the basis for this.

Q4. Which of the following best describes your employment status?

	%
Working – full time (30 or more hours a week)	51
Working – part-time (less than 30 hours a week)	18
Self-employed	5
Unemployed – looking for a job	3
Unemployed – not looking for a job/long-term sick or disabled/Housewife/husband/Full-time carer	22
Retired	*
Pupil/Student/In full-time education	1
NET: Working	74
NET: Not working	26

Q5. Is [Specified Child] a:

	%
Boy	49
Girl	51

Q6. Is [Specified Child] your first child?

	%
Yes	54
No	47

Q7. Have you or [Specified Child] ever been diagnosed by a medical doctor as having any long-lasting illness, disability or infirmity?

	You %	Specified Child %
Breathing complaint (e.g. asthma, bronchitis, pulmonary disease, emphysema)	14	11
Cancer	1	1
Diabetes	3	1
Heart disease (e.g. heart failure, high blood pressure)	2	1
Kidney disease (e.g. renal failure, kidney transplant)	1	1
Liver disease (e.g. hepatitis, cirrhosis)	1	1
Mental health (e.g. depression, anxiety, stress)	16	1
Neurological condition (i.e. caused by damage to the brain, spinal cord or other parts of the nervous system)	2	1
Stroke (or transient ischaemic attack; TIA)	*	*
Substance misuse (i.e. alcohol, drugs)	1	N/A
Other (please specify)	3	3
None	67	82
Don't know	1	1

Q8. To what extent, if at all, do you agree or disagree with the following statement.

***Flu would be a serious illness for*:**

	Specified Child %	You %	Someone in [Specified Child]'s household %
Strongly agree	33	20	22
Tend to agree	28	28	28
Neither agree nor disagree	18	22	21
Tend to disagree	12	17	14
Strongly disagree	6	9	8
Don't know/not sure	4	4	7

The next questions are all about [Specified Child] and the flu vaccine. Please answer yes, no or don't know for each question.

Q9. Has [Specified Child] had a flu vaccination at any time before 31st August 2015?

	%
Yes	55
No	40
Don't know	5

Q10. As far as you know, was [Specified Child] eligible to have a free flu vaccination this winter (2015/16)?

	%
Yes	71
No	12
Don't know	18

Q11. Has [Specified Child] had the flu vaccination this winter (2015/16)?

	%
Yes	52
No	44
Don't know	3

If 'Yes' go to question 12. If 'No' go to question 13.

Q12. Why did you decide to vaccinate [Specified Child] against flu? Please give us your main reason(s).

	%
I wanted to protect [Specified Child] from flu	61
I had an invitation/letter from [Specified Child]'s GP/school	57
I believe/am aware that [Specified Child] is in an at-risk group/more vulnerable	25
[Specified Child] always has it	23
The GP says [Specified Child] needs it	19
Other (Please specify)[1]	3
Don't know	0

Base: All those whose child had the child flu vaccination this Winter (n=526)

Go to question 14.

Q13. Why did you decide *not* to vaccinate [Specified Child] against flu? Please give us your main reason(s).

	%
[Specified Child] is generally healthy and I am not overly concerned about him/her catching flu	43
Side effects/it makes you ill/it causes flu or a bad reaction	22
I don't know enough about the vaccine	21
I am concerned over how safe the vaccine is/it hasn't been tested enough	20
Other (please specify)1	20
[Specified Child] doesn't need it	17
I don't like [Specified Child] having vaccinations	12
Don't know	4

Base: All those whose child did not have the child flu vaccination this Winter (n=402)

Go to question 17.

Q14. Did [Specified Child] experience any of the following side-effects because of the child flu vaccine?

	%
No, none	59
Runny or stuffy nose	16
Feeling tired, or having low energy	9
Fever	8
Generally unwell or not themselves	7
Headache	6
Flu	6
Reduced appetite	4
Weakness	4
Muscle aches	4
Pain in arms, legs or other joints	4
Nosebleed	3
Stomach pain	3
Nausea (feeling sick), gas or indigestion	3
Trouble sleeping	3
Dizziness	2
Rash	2
Chest pain	2
Shortness of breath	2
Back pain	1
Fainting spells	1
Feeling of heart pounding or racing	1
Constipation, loose bowels or diarrhoea	1
Allergic reactions	1
Other (please specify)	1

One or more side-effects	41

Base: All those whose child had the child flu vaccination this Winter (526)

If 'No, none' go to question 17.

Q15. Overall, how severe were the side-effects that [Specified Child] experienced?

	%
Very mild	24
Mild	55
Moderate	18
Severe	2
Don't know	1

Base: All those whose child had the child flu vaccination this Winter and experienced one or more side-effects (216)

Q16. Overall how worried were you, if at all, about the side-effects?

	%
Very worried	10
Fairly worried	31
Not very worried	38
Not at all worried	22
Don't know	0

Base: All those whose child had the child flu vaccination this Winter and experienced one or more side-effects (216)

Q17. How much input did you have in the vaccination decision for [Specified Child]?

	%
I had sole responsibility	37
I had joint responsibility, along with someone else	61
I had no responsibility	2
Other (please specify)	1
Don't know	0

Base: All those whose child had the child flu vaccination this Winter (526)

Think about next flu season (September 2016 – March 2017). During this time, you may be invited to vaccinate [Specified Child] against flu. For the following questions, please think about the next flu season.

For each of the following statements, please tell us to what extent, if at all, you agree or disagree:

Q18. I <u>want</u> [Specified Child] to be vaccinated for flu next year

	%
Strongly agree	37
Tend to agree	30
Neither agree nor disagree	14
Tend to disagree	8
Strongly disagree	8
Don't know/not sure	4

Q19. I <u>intend</u> [Specified Child] to be vaccinated for flu next year

	%
Strongly agree	37
Tend to agree	27
Neither agree nor disagree	14
Tend to disagree	9
Strongly disagree	9
Don't know/not sure	4

Q20. If I don't vaccinate [Specified Child], then [Specified Child] is likely to catch flu

	%
Strongly agree	10
Tend to agree	22
Neither agree nor disagree	35
Tend to disagree	20
Strongly disagree	7
Don't know/not sure	7

Q21. Below are some things that other people have said about the child flu vaccine. To what extent, if at all, do you agree or disagree with the following statements?

	I don't know enough about the child flu vaccine	The child flu vaccine has not been tested enough for me to feel it is safe	The child flu vaccine can cause unpleasant short-term side-effects	The child flu vaccine can cause long-term health problems
	%	%	%	%
Strongly agree	12	10	11	7
Tend to agree	26	16	34	12
Neither agree nor disagree	27	23	26	23
Tend to disagree	22	24	14	23
Strongly disagree	10	18	5	18
Don't know/not sure	2	9	10	17

Q22. Below are some more things that people have said about the child flu vaccine. To what extent, if at all, do you agree or disagree with the following statements?

	The child flu vaccine does not suit my religious or cultural beliefs/values	**The vaccination campaign is just about making money for the manufacturers**	**Having the child flu vaccine is an effective way of preventing [Specified Child] from catching flu**	**I don't like [Specified Child] having vaccinations in general**	**A health professional has recommended that [Specified Child] <u>should</u> be vaccinated**	**A health professional has recommended that [Specified Child] <u>shouldn't</u> be vaccinated**
	%	**%**	**%**	**%**	**%**	**%**
Strongly agree	5	8	21	7	14	6
Tend to agree	7	12	40	15	24	8
Neither agree nor disagreed	16	26	22	26	25	15
Tend to disagreed	11	23	7	22	14	17
Strongly disagreed	59	23	6	28	19	51
Don't know/not sure	3	8	4	2	5	4

Q23. Below are some more things that people have said about the child flu vaccine. To what extent, if at all, do you agree or disagree with the following statements?

	The flu vaccine would interact with other medications that [Specified Child] is currently taking	**Vaccinating [Specified Child] against flu each year will overload his/her immune system**	**Vaccinating [Specified Child] against flu each year is too much of an ongoing time commitment**	**A friend/relative has recommended that [Specified Child] <u>shouldn't</u> be vaccinated**	**Another child I know had side-effects from the vaccine**
	%	**%**	**%**	**%**	**%**
Strongly agree	4	6	6	5	6
Tend to agree	7	14	8	10	13
Neither agree nor disagree	15	22	19	17	17
Tend to disagree	15	18	18	16	14
Strongly disagree	54	29	46	49	42
Don't know/not sure	5	10	3	2	8

The following question is about your understanding of the effectiveness of vaccines. Please select the answer you think is most accurate. Please answer even if you are unsure.

Q24. If the child flu vaccine is 50% effective (this is just a made up number and is not how effective the child flu vaccine is in real life), does it mean that:

	%
50% of children who have the vaccine will be immune to flu	29
A vaccinated child will have a 50% chance of catching flu	27
If a child had a 50% chance of catching flu before being vaccinated, they now have half that chance (i.e. 25%)	19
Can't tell the difference between the options above	10
Don't know	15

The next four questions will ask you about some of the possible side-effects of the child flu vaccine. Please read the questions carefully, as many of them may seem very similar. If you are unsure, please give your best estimate. We are not expecting you to be accurate.

Q25. The child flu vaccine has severe allergic reaction as a listed side effect. The patient information leaflet mentions that:

Severe allergic reaction is a *very rare* side effect.

Imagine 10,000 children are vaccinated with the child flu vaccine. Out of these children, how many do you think will get a severe allergic reaction? Please type a number in the box below. If you are unsure, please provide your best estimate.

	%
0	*
1 - 100	73
101 - 500	10
501 - 1,000	8
1,001 - 2,500	3
2,501 - 5,000	4
5,001 – 8,000	1
8,001 – 10,000	1
Mean	516.8

Q26. The child flu vaccine has runny or stuffy nose as a listed side effect. The patient information leaflet mentions that:

Runny or stuffy nose is a *very common* side effect

Imagine 10,000 children are vaccinated with the child flu vaccine. Out of these children, how many do you think will get a runny or stuffy nose? Please type a number in the box below. If you are unsure, please provide your best estimate.

	%
0	0
1 - 100	16
101 - 500	6
501 - 1,000	14
1,001 - 2,500	6
2,501 - 5,000	20
5,001 – 7,500	11
7,501 – 10,000	28
Mean	4442.1

Q27. The child flu vaccine has fever as a listed side effect. The patient information leaflet mentions that:

Fever is a *common* side effect

Imagine 10,000 children are vaccinated with the child flu vaccine. Out of these children, how many do you think will get a fever? Please type a number in the box below. If you are unsure, please provide your best estimate.

	%
0	*
1 - 100	22
101 - 500	8
501 - 1,000	16
1,001 - 2,500	8
2,501 - 5,000	23
5,001 – 7,500	10
7,501 – 10,000	14
Mean	3359.5

Q28. The child flu vaccine has rash as a listed side effect. The patient information leaflet mentions that:

Rash is an *uncommon* side effect

Imagine 10,000 children are vaccinated with the child flu vaccine. Out of these children, how many do you think will get a rash? Please type a number in the box below. If you are unsure, please provide your best estimate.

	%
0	1
1 - 100	49
101 - 500	17
501 - 1,000	18
1,001 - 2,500	7
2,501 - 5,000	7
5,001 – 7,500	1
7,501 – 10,000	2
Mean	887

Q29. In which of the following categories would you place your total household income from all sources before tax and any other deductions?

	%
Under £10,000	5
£10,000 - £19,999	12
£20,000 - £29,999	19
£30,000 - £39,999	20
£40,000 - £49,999	16
£50,000 - £75,000	14
£75,000 or over	9
Don't know/Prefer not to say	6

Q30. Please tell us which, if any, is the highest educational or professional qualification you have obtained?

	%
GCSE/CSE/O-Level	13
Vocational qualifications (=NVQ1 or 2)	9
A-level or equivalent (=NVQ3)	23
Bachelor degree or equivalent (=NVQ4)	33
Masters degree or equivalent	16
PhD or equivalent	4
Other	1
No formal qualifications	1
Still studying	*
Don't know/Prefer not to say	1

Q31. Which one of these ethnic groups would you describe yourself as belonging to?

	%
White – English/Welsh/Scottish/Northern Irish/British	75
White – Irish	1
White – Gypsy or Irish Traveller	*
White – Any other background	9
Mixed or multiple ethnic groups – White and Black Caribbean	1
Mixed or multiple ethnic groups – White and Black African	1
Mixed or multiple ethnic groups – White and Asian	1
Mixed or multiple ethnic groups – Any other mixed/multiple ethnic background	1
Asian or Asian British – Indian	4
Asian or Asian British – Pakistani	2
Asian or Asian British – Bangladeshi	1
Asian or Asian British – Chinese	1
Asian or Asian British – Any other Asian background	1
Black, African, Caribbean or Black British – African	1
Black, African, Caribbean or Black British – Caribbean	*
Black, African, Caribbean or Black British – Any other Black/African/Caribbean background	*
Other ethnic group – Arab	*
Other ethnic group – Any other ethnic group	*
Prefer not to say	2
NET: White	84
NET: BME	14

Appendix 6. Scrambled sentence task

Instructions

In this section, you will be asked to complete a word sorting task. You will be asked to unscramble sentences to form statements. Each scrambled sentence contains six words. Unscramble five words in each sentence by dragging them into the boxes in the correct order. There are no right or wrong answers.

Try this practice question

child	green	has	the	eyes	blue

➔

the	child	has	blue	eyes

Try this practice question

Practise

the	windy	yesterday	weather	snowy	was

Thank you. You have completed the practise, and you will now be taken to the **main** task. Unscramble the sentences to form statements, not questions. Unscramble the sentences to form whatever statement comes to mind first. Work as quickly as you can, because your time will be limited to 2 minutes. If you make a mistake, simply move on to the next item.

Remembering the number

Before we start the word-sorting task, you will need to memorise a 6-digit number. You will be shown it for a few seconds then it will be hidden. After this you will be asked to input the number. When you have done that correctly a couple of times, we'll start the sentences. You will be given up to **five** attempts in total, before moving on to the word sorting exercise. When you click the 'next' button below, the number will be shown.

[Possible numbers: 720185, 615239]

Please keep the number in your mind.

Please input the number in the box below:

— — — — — —

Word sorting task instructions

You will now complete the word sorting task. Please keep the number in your mind while you unscramble the sentences, as you will be asked to recall it later. Please do not use any memory aides to help you to remember the number - it's important that you only use your own memory. Remember to work as quickly as you can because your time will be limited. **Once you have dragged a word into a box you will not be able to move it.**

Source of health threat

Man-made health threat items

1. very vaccines don't prevent illnesses well (vaccines)

Negative disambiguation: Vaccines don't prevent illnesses well

Positive disambiguation: Vaccines prevent illnesses very well

2. can protect people harm new inventions (new inventions)†

Negative disambiguation: New inventions can harm people

Positive disambiguation: New inventions can protect people

3. react badly medicines to I well (medicines)

Negative disambiguation: I react badly to medicines

Positive disambiguation: I react well to medicines

4. medicines me give side-effects often rarely (side-effects)

Negative disambiguation: Medicines often give me side-effects

Positive disambiguation: Medicines rarely give me side-effects

5. release phones harmless waves mobile dangerous (mobile phone waves)‡

Negative disambiguation: Mobile phones release dangerous waves

Positive disambiguation: Mobile phones release harmless waves

† Item not used in prospective cohort study. In the prospective cohort study, this item was replaced by:

products prevent illnesses cause household cleaning (household cleaning products)

Negative disambiguation: Household cleaning products cause illnesses

Positive disambiguation: Household cleaning products prevent illnesses

‡ Item not used in prospective cohort study. In the prospective cohort study, this item was replaced by:

signals phone harmless dangerous mobile are (mobile phone waves)

Negative disambiguation: Mobile phones signals are dangerous

Positive disambiguation: Mobile phones signals are harmless

Naturally-occurring health threat items

1. illness a flu serious is minor (influenza)

Negative disambiguation: Flu is a serious illness

Positive disambiguation: Flu is a minor illness

2. about regularly illnesses I seldom worry (illness)

Negative disambiguation: I regularly worry about illness

Positive disambiguation: I seldom worry about illness

3. harmful bacteria contained be cannot can (bacteria)§

Negative disambiguation: Harmful bacteria cannot be contained

Positive disambiguation: Harmful bacteria can be contained

4. people frequently make germs ill occasionally (germs)‖

Negative disambiguation: Germs frequently make people ill

Positive disambiguation: Germs occasionally make people ill

5. suntan getting a is enjoyable damaging (sun exposure)

Negative disambiguation: Getting a suntan is damaging

Positive disambiguation: Getting a suntan is enjoyable

§ Item not used in prospective cohort study. In the prospective cohort study, this item was replaced by:

bacteria are harmful quite usually helpful (bacteria)

Negative disambiguation: Bacteria are usually quite harmful

Positive disambiguation: Bacteria are usually quite helpful

‖ Item not used in prospective cohort study. In the prospective cohort study, this item was replaced by:

contain nutrients plats most poisons wild (wild plants)

Negative disambiguation: Most wild plants contain poisons

Positive disambiguation: Most wild plants contain nutrients

Subject of health threat

Self-relevant health threat items

1. physical my health bad is good (physical health)

Negative disambiguation: My physical health is bad

Positive disambiguation: My physical health is good

2. feel usually healthy very I tired (energy level)

Negative disambiguation: I usually feel very tired

Positive disambiguation: I usually feel very healthy

3. mostly my health poor fine is (general health)

Negative disambiguation: My health is mostly poor

Positive disambiguation: My health is mostly fine

4. abnormal aches are harmless usually most (aches)

Negative disambiguation: Most aches are usually abnormal

Positive disambiguation: Most aches are usually harmless

5. experiencing physical worrying is normal pain (pains)

Negative disambiguation: Experiencing physical pain is worrying

Positive disambiguation: Experiencing physical pain is normal

Child-relevant health threat items

1. is child normally my tired energetic (energy level)

Negative disambiguation: My child is normally tired

Positive disambiguation: My child is normally energetic

2. good health child's my is worrying (general health)

Negative disambiguation: My child's health is worrying

Positive disambiguation: My child's health is good

3. my strong is weak child physically (physical strength)

Negative disambiguation: My child is physically weak

Positive disambiguation: My child is physically strong

4. damaging children in common is illness (illness)

Negative disambiguation: Illness is damaging in children

Positive disambiguation: Illness is common in children

5. is development delayed healthy my child's (development)

Negative disambiguation: My child's development is delayed

Positive disambiguation: My child's development is health

Appendix 7. Table of reasons given by participants for vaccinating the child

Reasons for vaccinating child		Reasons for not vaccinating child	
Reason	Number of parents (%)[5] – total n=526	Reason	Number of parents (%) – total n=438
I wanted to protect [child] from flu	322 (61.2)	[Child] is generally healthy and I am not overly concerned about him/her catching flu	189 (43.2)
I had an invitation/letter from [child]'s GP/school	301 (57.2)	Side-effects/it makes you ill/it causes flu or a bad reaction	95 (21.7)
I believe/am aware that [child] is in an at-risk group/more vulnerable	132 (25.1)	I don't know enough about the vaccine	93 (21.2)
[Child] always has it	123 (23.4)	I am concerned over how safe the vaccine is/it hasn't been tested enough	90 (20.5)
The GP says [child] needs it	101 (19.2)	[Child] doesn't need it	74 (16.9)
Other	9 (1.7)	I don't like [child] having vaccinations	53 (12.1)
Don't know	0 (0.0)	Other	86 (19.6)
		Don't know	19 (4.3)

Abbreviations: GP – general practice

[5] Three participants indicated that they had answered the vaccination question incorrectly and that they had indeed vaccinated their child; these participants' results were recoded. However, due to scripting of the questionnaire, only participants who indicated that their child had been vaccinated were asked why they had chosen to vaccinate their child. Therefore, data about reasons for vaccinating the child is for 526 participants.

Appendix 8. Table showing side-effects perceived by parents as a result of the influenza vaccine

Side-effect perceived	Number of parents (%)
None	310 (59.0)
Runny or stuffy nose	84 (16.0)
Feeling tired, or having low energy	49 (9.3)
Fever	42 (8.0)
Generally unwell or not themselves	37 (7.0)
Flu	33 (6.3)
Headache	30 (5.7)
Reduced appetite	23 (4.4)
Muscle aches	23 (4.4)
Weakness	19 (3.6)
Pain in arms, legs or other joints	19 (3.6)
Nausea (feeling sick), gas or indigestion	18 (3.4)
Trouble sleeping	16 (3.0)
Nosebleed	15 (2.9)
Stomach pain	14 (2.7)
Rash	11 (2.1)
Shortness of breath	11 (2.1)
Chest pain	10 (1.9)
Dizziness	8 (1.5)
Back pain	8 (1.5)
Feeling of heart pounding or racing	8 (1.5)
Constipation, loose bowels or diarrhoea	7 (1.3)
Fainting spells	6 (1.1)
Allergic reactions	6 (1.1)
Other	1 (0.2)
One or more side-effects	215 (41.0)

Appendix 9. Personal and clinical characteristics of those assigned to receive items pertaining to source and subject of the health threat; and those who were and were not included in the interpretation bias analyses in the cross-sectional study

		Assigned to source or subject of health threat items			Source of health threat			Subject of health threat		
		Source of health threat (n=500), n (%)	Subject of health threat (n=501), n (%)	p	Included in analyses (n=158), n (%)	Not included in analyses (n=342), n (%)	p	Included in analyses (n=163), n (%)	Not included in analyses (n=338), n (%)	p
Parent gender	Female	288 (50.3)	285 (49.7)	.82	90 (31.3)	198 (68.8)	.84	95 (33.3)	190 (66.7)	.66
	Male	212 (49.5)	216 (50.5)		68 (32.1)	144 (67.9)		68 (31.5)	148 (68.5)	
Parent age	35+	294 (49.7)	298 (50.3)	.83	89 (30.3)	205 (69.7)	.45	94 (31.5)	204 (68.5)	.57
	18-34	206 (50.4)	203 (49.6)		69 (33.5)	137 (66.5)		69 (34.0)	134 (66.0)	
Region	North East	26 (51.0)	25 (49.0)	.99	7 (26.9)	19 (73.1)	.49	9 (36.0)	16 (64.0)	.57
	North West	63 (49.6)	64 (50.4)		19 (30.2)	44 (69.8)		23 (35.9)	41 (64.1)	
	Yorkshire and Humberside	54 (46.2)	63 (53.8)		14 (25.9)	40 (74.1)		27 (42.9)	36 (57.1)	
	West Midlands	57 (53.8)	49 (46.2)		16 (28.1)	41 (71.9)		17 (34.7)	32 (65.3)	
	East Midlands	47 (49.0)	49 (51.0)		12 (25.5)	35 (74.5)		17 (34.7)	32 (65.3)	
	East of England	39 (50.6)	38 (49.4)		10 (25.6)	29 (74.4)		11 (28.9)	27 (71.1)	
	South West	56 (50.5)	55 (49.5)		19 (33.9)	37 (66.1)		14 (25.5)	41 (74.5)	
	South East	84 (49.4)	86 (50.6)		35 (41.7)	49 (58.3)		26 (30.2)	60 (69.8)	
	London	74 (50.7)	72 (49.3)		26 (35.1)	48 (64.9)		19 (26.4)	53 (73.6)	
Parent employment	Working	375 (49.3)	386 (50.7)	.45	116 (30.9)	259 (69.1)	.58	131 (33.9)	255 (66.1)	.22
	Not working	125 (52.1)	115 (47.9)		42 (33.6)	83 (66.4)		32 (27.8)	83 (72.2)	
Total household	≥£30,000	297 (50.4)	292 (49.6)	.87	104 (35.0)	193 (65.0)	.05*	90 (30.8)	202 (69.2)	.60
	Under £30,000	179 (51.0)	172 (49.0)		47 (26.3)	132 (73.7)		57 (33.1)	115 (66.9)	

income before tax and other deductions										
Parent highest educational or professional qualification‡	Degree or higher (Bachelors, Masters, PhD)	273 (50.9)	263 (49.1)	.67	90 (33.0)	193 (67.0)	.58	82 (31.2)	181 (68.8)	.50
	GCSE/vocational/A-level/No formal qualifications	219 (49.5)	223 (50.5)		67 (30.6)	152 (69.4)		76 (34.1)	147 (65.9)	
Parent ethnicity	Black and Minority	77 (55.0)	63 (45.0)	.21	12 (15.6)	65 (84.4)	.001*	13 (20.6)	50 (79.4)	.03*
	White	414 (49.2)	427 (50.8)		144 (34.8)	270 (65.2)		147 (34.4)	280 (65.6)	
Parent chronic illness	Present	167 (52.0)	154 (48.0)	.39	57 (34.1)	110 (65.9)	.41	46 (29.9)	108 (70.1)	.39
	None	331 (49.1)	343 (50.9)		101 (30.5)	230 (69.5)		116 (33.8)	227 (66.2)	
Child gender	Female	261 (51.1)	250 (48.9)	.47	86 (33.0)	175 (67.0)	.50	75 (30.0)	175 (70.0)	.23
	Male	239 (48.8)	251 (51.2)		72 (30.1)	167 (69.9)		88 (35.1)	163 (64.9)	
First-born child	Yes	270 (50.2)	268 (49.8)	.87	81 (30.0)	189 (70.0)	.40	89 (33.2)	179 (66.8)	.73
	No	230 (49.7)	233 (50.3)		77 (33.5)	153 (66.5)		74 (31.8)	159 (68.2)	
Child age	2 to 7 years	N=500, M=4.62, SD=1.632	N=501, M=4.39, SD=1.725	.02*	N=158, M=4.58, SD=1.690	N=342, M=4.67, SD=1.606	.58	N=163, M=4.34, SD=1.711	N=228, M=4.42, SD=1.733	.62
Child chronic illness	Present	82 (50.6)	80 (49.4)	.83	28 (34.1)	54 (68.2)	.62	28 (35.0)	52 (65.0)	.63
	None	411 (49.7)	416 (50.3)		129 (31.4)	282 (68.6)		134 (32.2)	282 (67.8)	

*$p \leq .05$

Appendix 10. T1 questionnaire

- Results are based on all respondents (n=270) unless otherwise stated.
- Where percentages do not sum to 100, this may be due to respondents being able to select multiple responses, computer rounding or the exclusion of 'don't know.'
- An asterisk (*) represents a value of less than half or one percent, but greater than zero.

Please state:

Q1. Child's name

Q2. Is [Specified child] a:

	%
Boy	46
Girl	54

Base: n=269

Q3. What is [Specified child]'s date of birth?

Day:

Month:

Year:

Q4. What is your relationship to [Specified child]?

	%
Mother	81
Father	18
Other, please state	1

Base: n=269

Q5. How likely do you think it is that [Specified child] will get short term side-effects from the flu vaccine?

	%
Very likely	6
Likely	32
Neither likely nor unlikely	34
Unlikely	25
Very unlikely	3

Base: n=268

Q6. These questions relate to your child's sensitivity to medicines. To what extent, if at all, do you agree or disagree with the following statement?

	[Specified child]'s body is very sensitive to medicines	[Specified child]'s body overreacts to medicines	[Specified child] usually has a stronger reaction to medicines than most other children I know	[Specified child] has had a bad reaction to medicines in the past	Even small amounts of medicine can upset [Specified child]'s body
	%	%	%	%	%
Strongly agree	*	*	1	2	1
Agree	7	2	2	5	*
Neutral	36	25	18	9	13
Disagree	41	49	52	46	49
Strongly disagree	16	24	27	39	37

Q7. The healthcare worker vaccinating your child is a possible source of information about the child flu vaccine. Considering what you know, please

select the number between the pair of words that best describes your feelings about information from the healthcare worker vaccinating your child.

	1 %	**2 %**	**3 %**	**4 %**	**5 %**	
Can't be trusted	1	0	8	35	56	Can be trusted
Is inaccurate	1	0	12	35	53	Is accurate
Is unfair	2	0	9	33	57	Is fair
Doesn't tell the whole story	*	2	16	37	46	Tells the whole story
Is biased	1	4	18	33	44	Is unbiased

Base: Can be trusted, n=269; is accurate, n=267; is fair, n=266; tells the whole story, n=268; is unbiased, n=267

Q8. To what extent do you agree or disagree that you trust the following as a source of information about the flu vaccine

	Friends/family/relatives (people I speak to everyday) %	Official websites/helplines/departments/agencies %	Media (radio/website/tv/newspapers/adverts) %	NHS flu vaccination leaflet %
Strongly disagree	2	2	3	2
Tend to disagree	11	3	14	3
Neither agree nor disagree	37	13	47	10
Tend to agree	37	41	25	29
Strongly agree	9	36	4	50
I have never had information from this source	5	5	7	5

Base: NHS influenza vaccination leaflet, n=269.

Q9. We are interested in what you think each of the following said about the likelihood of the flu vaccine causing side-effects. Please tick one box for each source of information.

	Friends/family/relatives (people I speak to everyday) %	Official websites/helplines/departments/agencies %	Media (radio/website/tv/newspapers/adverts) %	NHS flu vaccination leaflet %
They said side-effects were very likely	4	2	5	3
They said side-effects were likely	28	18	20	21
They said side-effects were unlikely	25	37	24	36
They said side-effects were very unlikely	8	14	7	15
I have never had information from this source	35	30	45	26

Base: Friends/family/relatives, n=268; official websites/helplines/departments/agencies, n=267; media, n=267; NHS influenza vaccination leaflet, n=268

Q10. Not including [Specified child], do you know any children who have experienced side-effects from the flu vaccine?

	%
Yes, several other children I know had side-effects from the flu vaccine	86
Yes, one other child I know had side-effects from the flu vaccine	7
No, I don't know any children who had side-effects from the flu vaccine	6

Base: n=269

If 'Yes' go to question 11. If 'No' go to question 12.

Q11. Overall, how severe were the side-effects that the child or children you know experienced after the flu vaccine?

	%
Very mild	11
Mild	70
Moderate	14
Severe	5
Very severe	0

Base: All those who indicated they knew another child who had experienced side-effects from the influenza vaccine, n=37

Q12. Below are some things that other people have said about the child flu vaccine. To what extent, if at all, do you agree or disagree with the following statements? Please select one answer option for each statement.

	The child flu vaccine has not been tested enough for me to feel it is safe	The child flu vaccine can cause unpleasant short-term side effects	The child flu vaccine can cause long-term health problems	The child flu vaccine does not suit my religious or cultural beliefs/values
	%	%	%	%
Strongly agree	2	2	1	2.2
Tend to agree	5	16	1	1
Neither agree nor disagree	30	43	27	19
Tend to disagree	33	29	29	10
Strongly disagree	30	11	42	69

Q13. Below are some things that other people have said about the child flu vaccine. To what extent, if at all, do you agree or disagree with the following statements? Please select one answer option for each statement.

	I don't like [Specified child] having vaccinations in general	I don't know enough about the child flu vaccine	The vaccination campaign is just about making money for the manufacturers	The flu vaccine would interact with other medications that [Specified child] is currently taking
	%	%	%	%
Strongly agree	1	4	2	0
Tend to agree	3	18	2	1
Neither agree nor disagree	17	32	23	26
Tend to disagree	27	32	34	27
Strongly disagree	52	15	39	46

Base: The vaccination campaign is just about making money for the manufacturers, n=269; the flu vaccine would interact with other medications that [Specified child] is currently taking, n=268

Q14. Below are some things that other people have said about the child flu vaccine. To what extent, if at all, do you agree or disagree with the following statements? Please select one answer option for each statement.

	Vaccinating [Specified child] against flu each year will overload his/her immune system	Vaccinating [Specified child] against flu each year is too much of an ongoing time commitment	Having the child flu vaccine is an effective way of preventing [Specified child] from catching flu	If I don't vaccinate [Specified child], then [Specified child] will get flu
	%	%	%	%
Strongly agree	2	1	29	3
Tend to agree	4	3	51	21
Neither agree nor disagree	20	14	12	45
Tend to disagree	42	27	6	24
Strongly disagree	33	56	3	7

Base: If I don't vaccinate [Specified child], then [Specified child] will get flu, n=269

Q15. Has [Specified child] had the flu vaccine at any time before 31st August 2016?

	%
Yes	49
No	47
Don’t know	4

If ‘Yes’ go to question 16. If ‘No’ or ‘Don’t know’ go to question 19.

Q16. Children sometimes experience side-effects after a vaccine (for example, a runny nose, headache or temperature). Has [Specified child] ever had side-effects from the flu vaccine before?

	%
Yes	21
No	59
Don't know	20

Base: All those who indicated their child had previously been vaccinated for influenza, n=131

If 'Yes' go to question 17. If 'No' or 'Don't know' go to question 19.

Q17. Overall, how severe were the side-effects that [Specified child] experienced as a result of the flu vaccine?

	%
Very mild	46
Mild	43
Moderate	11
Severe	0
Very severe	0

Base: All those who indicated their child had previously experienced side-effects from the child influenza vaccine, n=28

Q18. Overall, how worried were you about the side-effects that [Specified child] got after previous flu vaccinations?

	%
Not at all worried	50
Not very worried	29
Fairly worried	18
Very worried	4

Base: All those who indicated their child had previously experienced side-effects from the child influenza vaccine, n=28

Q19. Has [Specified child] ever had side-effects from any other routine vaccine (i.e. NOT the child flu vaccine)?

	%
Yes	41
No	49
Don't know	9

Base: n=269

If 'Yes' go to question 20. If 'No' or 'Don't know go to question 21.

Q20. Overall, how worried were you about the side-effects that [Specified child] got?

	%
Not at all worried	32
Not very worried	53
Fairly worried	14
Very worried	1

Base: All those who indicated their child had previously experienced side-effects from any other routine vaccination, n=111

Q21. Has [Specified child] shown signs of any of the following symptoms in the last 24 hours?

	%
No, none	63
Runny or stuffy nose	22
Feeling tired, or having low energy	4
Fever	4
Generally unwell or not themselves	3
Headache	1
Flu	1
Reduced appetite	2
Weakness	*
Muscle aches	1
Pain in arms, legs or other joints	1
Nosebleed	*
Stomach pain	2
Nausea (feeling sick), gas or indigestion	*
Trouble sleeping	3
Dizziness	*
Rash	1
Chest pain	0
Shortness of breath	0
Back pain	0
Fainting spells	0
Feeling of heart pounding or racing	0
Constipation, loose bowels or diarrhoea	2
Allergic reactions	0
Other (please specify)	6
One or more side-effects	37

Base: n=260

Appendix 11. T2 questionnaire

- Results are based on all respondents (n=233) unless otherwise stated.
- Where percentages do not sum to 100, this may be due to respondents being able to select multiple responses, computer rounding or the exclusion of 'don't know.'
- An asterisk (*) represents a value of less than half or one percent, but greater than zero.

Q1. Do you think that [Specified child] experienced any of the following side-effects because of their latest child flu vaccine? Tick all that apply.

	%
No, none	57
Runny or stuffy nose	23
Feeling tired, or having low energy	15
Fever	8
Generally unwell or not themselves	6
Headache	2
Flu	2
Reduced appetite	6
Weakness	1
Muscle aches	1
Pain in arms, legs or other joints	0
Nosebleed	1
Stomach pain	2
Nausea (feeling sick), gas or indigestion	1
Trouble sleeping	4
Dizziness	*
Rash	1
Chest pain	0
Shortness of breath	*
Back pain	0
Fainting spells	0
Feeling of heart pounding or racing	*
Constipation, loose bowels or diarrhoea	3
Allergic reactions	0
Other (please specify)	3
One or more side-effects	43

Base: n=221

If 'No, none' go to question 4.

Q2. Overall, how severe were the side-effects that [Specified child] experienced from their latest flu vaccine?

	%
Very mild	40
Mild	38
Moderate	19
Severe	2
Very severe	1

Base: All those who perceived their child to experience side-effects from the child influenza vaccine, n=100

Q3. How worried were you about the overall side-effects that [Specified child] experienced from their latest flu vaccine?

	%
Not at all worried	50
Not very worried	38
Fairly worried	10
Very worried	2

Base: All those who perceived their child to experience side-effects from the child influenza vaccine, n=100

Think about next flu season (September 2017 to March 2018). You will be asked to vaccinate [Specified child] against flu again. The following questions relate to the 2017/18 flu season.

Q4. I want [Specified child] to be vaccinated for flu next year

	%
Strongly agree	47
Agree	41
Neither agree nor disagree	8
Disagree	0
Strongly disagree	4

Base: n=228

Q5. I intend [Specified child] to be vaccinated for flu next year

	%
Strongly agree	49
Agree	40
Neither agree nor disagree	8
Disagree	*
Strongly disagree	3

Base: n=228

These questions relate to [Specified child]'s recent flu vaccination appointment. To what extent, if at all, do you agree or disagree with the following statement?

Q6. The healthcare worker who vaccinated [Specified child] can be trusted as a source of information about the flu vaccine

	%
Strongly agree	37
Agree	51
Neither agree nor disagree	8
Disagree	1
Strongly disagree	2

Base: n=216

Q7. In your flu vaccine appointment, did the healthcare worker suggest that the flu vaccine might cause side-effects?

	%
Yes, they said side-effects were very likely	2
Yes, they said side-effects were likely	33
No, they didn't mention side-effects	39
No, they said that side-effects were unlikely	20
No, they said that side-effects were very unlikely	6

Base: n=216

Q8. In addition to children, the flu vaccine is recommended to certain 'at risk' groups. Aside from any children born between September 1st 2011 and August 31st 2014, is there anyone currently living in your household who is eligible for the flu vaccine in order to protect their health?

	%
Yes	38
No	53
Don't know	10

Base: n=216

Q9. Is [Specified child] your first child?

	%
Yes	38
No	62

Base: n=216

Q10. Have you ever been diagnosed by a medical doctor as having any long-lasting illness, disability or infirmity?

	%
Breathing complaint (e.g. asthma, bronchitis, pulmonary disease, emphysema)	9
Cancer	1
Diabetes	1
Heart disease (e.g. heart failure, high blood pressure)	1
Kidney disease (e.g. renal failure, kidney transplant)	0
Liver disease (e.g. hepatitis, cirrhosis)	0
Mental health (i.e. depression, anxiety, stress)	9
Neurological condition (i.e. caused by disease or damage to the brain, spinal cord or other parts of the nervous system)	0
Stroke (or transient ischaemic attack; TIA)	0
Substance misuse (i.e. alcohol, drugs)	0
Other, please specify	4
No	77
Don't know	1
Parent presence of chronic illness	23

Base: n=216

Q11. Has [Specified child] ever been diagnosed by a medical doctor as having any long-lasting illness, disability or infirmity?

	%
Breathing complaint (e.g. asthma, bronchitis, pulmonary disease, emphysema)	6
Cancer	0
Diabetes	0
Heart disease (e.g. heart failure, high blood pressure)	1
Kidney disease (e.g. renal failure, kidney transplant)	0
Liver disease (e.g. hepatitis, cirrhosis)	0
Mental health (i.e. depression, anxiety, stress)	0
Neurological condition (i.e. caused by disease or damage to the brain, spinal cord or other parts of the nervous system)	0
Stroke (or transient ischaemic attack; TIA)	0
Other, please specify	3
No	92
Don't know	0
Child presence of chronic illness	8

Base: n=216

Q12. To what extent, if at all, do you agree or disagree with the following statement. Flu would be a serious illness for:

	Specified Child	You	Someone in [Specified Child]'s household
	%	%	%
Strongly agree	20	15	21
Tend to agree	45	33	37
Neither agree nor disagree	20	26	21
Tend to disagree	13	20	14
Strongly disagree	3	7	7

Base: n=215

Q13. If [Specified child] were to catch flu, how much, if at all, would it impact your daily life?

	%
Not at all	2
Very little	2
Somewhat	50
A great extent	47

Base: n=215

Q14. To the best of your knowledge, is [Specified child] up-to-date with other routine vaccines?

	%
Yes, [Specified child] has completed all routine vaccines	95
[Specified child] is partially up-to-date	5
[Specified child] has not had any routine vaccines	0
Don't know	0

Base: n=214

Q15. How much input did you have in the vaccination decision for [Specified child]?

	%
I had sole responsibility	24
I had joint responsibility, along with someone else	77
I had no responsibility	0

Base: n=213

Q16. We would like to ask you about your personal views about medicines in general. These are statements other people have made about medicines in general. Please indicate the extent to which you agree or disagree with them by ticking the appropriate box. There are no right or wrong answers; we are interested in your personal views.

	Doctors use too many medicines	People who take medicines should stop their treatment for a while every now and then	Most medicines are addictive	Natural remedies are safer than medicines	Medicines do more harm than good	All medicines are poisons	Doctors place too much trust in medicines	If doctors had more time with patients they would prescribe fewer medicines
	%	%	%	%	%	%	%	%
Strongly agree	2	1	18	1	1	1	1	6
Agree	23	12	42	10	1	1	9	34
Neither agree nor disagree	36	40	32	36	25	15	29	34
Disagree	34	33	8	33	49	39	46	21
Strongly disagree	5	14	1	20	24	45	15	5

Base: n=214

Q17. A number of statements which people have used to describe themselves are given below. Read each statement and then choose the most appropriate statement to indicate how you generally feel. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe your feelings best.

	I feel calm %	I am tense %	I feel upset %	I am relaxed %	I feel content %	I am worried %
Almost never	1	9	25	3	2	10
Sometimes	35	72	71	40	24	70
Often	53	18	4	50	48	17
Almost always	11	1	0	7	26	3

Base: n=213

Q18. Please answer each question by selecting either the 'Yes' or the 'No' following the question. There are no right or wrong answers, and no trick questions. Work quickly and do not think too long about the exact meaning of the questions.

	Does your mood often go up and down? %	Do you often feel 'fed-up'? %	Would you call yourself a nervous person? %	Are you a worrier? %	Do you suffer from 'nerves'? %	Do you often feel lonely? %
Yes	43	33	16	53	12	9
No	57	67	84	47	88	91

Base: n=213

Q19. This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. Indicate the extent you have felt this way over the past week.

	Distressed %	Excited %	Upset %	Scared %	Enthusiastic %	Alert %	Inspired %	Nervous %	Determined %	Afraid %
Very slightly or not at all	59	14	42	79	8	6	8	51	8	77
A little	25	24	40	14	19	9	21	36	14	17
Moderately	12	40	14	7	39	41	36	9	30	5
Quite a bit	4	20	4	0	32	36	34	4	35	1
Extremely	0	1	0	0	2	9	2	1	13	0

Base: n=209

Q20. These days many people worry about the effects of different aspects of modern life on health. Please rate the following items for how much you are concerned about their effect on your personal health. Tick one box for each item.

	Cell phones	Radio or cell phone towers	High tension power lines	Nuclear radiation	Air pollution	Noise pollution	Depletion of the ozone layer
	%	%	%	%	%	%	%
No concern	34	47	55	35	5	32	14
A little concern	41	32	28	26	24	26	29
Moderate concern	17	18	13	18	33	24	26
High concern	7	3	4	14	32	15	24
Extreme concern	0	0	0	6	7	3	7

	Traffic fumes	Other environmental pollution	Pesticide spray	Poor building ventilation	Genetically modified food	Additives in food	Pesticides in food
	%	%	%	%	%	%	%
No concern	4	9	18	29	29	11	10
A little concern	20	26	33	26	29	28	30
Moderate concern	32	36	26	27	22	31	29
High concern	35	25	17	15	16	22	22
Extreme concern	9	5	6	2	5	7	10

	Antibiotics in food	Hormones in food	Mad cow disease	Contaminated water supply	Flouridation of water	Vaccination programmes	Overuse of antibiotics
	%	%	%	%	%	%	%
No concern	18	16	39	37	49	62	14
A little concern	22	23	24	22	26	24	25
Moderate concern	20	23	16	17	12	11	29

High concern	30	26	14	14	11	3	24
Extreme concern	10	12	7	10	3	1	9

	Toxic chemicals in household products	**Leakage from microwave ovens**	**Bacteria in air conditioning systems**	**Drug resistant bacteria**	**Mercury dental fillings**	**Medical and dental x-rays**	**Bio-terrorism (e.g. anthrax poisoning)**
	%	**%**	**%**	**%**	**%**	**%**	**%**
No concern	16	47	41	13	55	54	35
A little concern	34	26	31	22	23	33	26
Moderate concern	30	15	18	27	17	13	24
High concern	16	9	9	24	4	1	10
Extreme concern	4	3	2	14	1	0	6

Base: n=208

Q21. Please be as honest and accurate as you can throughout. Try not to let your response to one statement influence your responses to other statements. There are no "correct" or "incorrect" answers. Answer according to your own feelings, rather than how you think "most people" would answer

	In uncertain times, I usually expect the best	It's easy for me to relax	If something can go wrong for me, it will	I'm always optimistic about my future	I enjoy my friends a lot	It's important for me to keep busy	I hardly ever expect things to go my way	I don't get upset too easily	I rarely count on good things happening to me	Overall, I expect more good things to happen to me than bad
	%	**%**	**%**	**%**	**%**	**%**	**%**	**%**	**%**	**%**
Strongly agree	3	3	12	5	25	13	1	5	1	11
Agree	39	39	45	51	60	58	9	31	9	55
Neither agree nor disagree	38	35	36	31	12	21	31	35	33	24
Disagree	18	22	6	12	4	7	47	28	45	7
Strongly disagree	2	2	2	1	0	1	12	2	12	2

Base: n=202

Q22. Your age (in years) on your last birthday:

Q23. The gender you identify yourself with:

	%
Male	18
Female	82

Base: n=270

Appendix 12. T3 questionnaire

- Results are based on all respondents (n=200) unless otherwise stated.
- Where percentages do not sum to 100, this may be due to respondents being able to select multiple responses, computer rounding or the exclusion of 'don't know.'
- An asterisk (*) represents a value of less than half or one percent, but greater than zero.

Q1. Do you think that [Specified child] experienced any of the following side-effects because of their latest child flu vaccine? Tick all that apply

	%
No, none	64
Runny or stuffy nose	22
Feeling tired, or having low energy	8
Fever	10
Generally unwell or not themselves	6
Headache	1
Flu	3
Reduced appetite	6
Weakness	1
Muscle aches	0
Pain in arms, legs or other joints	1
Nosebleed	1
Stomach pain	1
Nausea (feeling sick), gas or indigestion	1
Trouble sleeping	3
Dizziness	0
Rash	1
Chest pain	0
Shortness of breath	0
Back pain	0
Fainting spells	0
Feeling of heart pounding or racing	0
Constipation, loose bowels or diarrhoea	2
Allergic reactions	0
Other (please specify)	1
One or more side-effects	36

If 'No' go to question 4.

Q2. Overall, how severe were the side-effects that [Specified child] experienced from their latest flu vaccine?

	%
Very mild	39
Mild	38
Moderate	20
Severe	3
Very severe	0

Base: All those who perceived their child to experience side-effects from the child influenza vaccine, n=66

Q3. How worried were you about the overall side-effects that [Specified child] experienced from their latest flu vaccine?

	%
Not at all worried	50
Not very worried	37
Fairly worried	11
Very worried	1

Base: All those who perceived their child to experience side-effects from the child influenza vaccine, n=70

Think about next flu season (September 2017 - March 2018). You will be asked to vaccinate [Specified child] against flu again. The following questions relate to the 2017/18 flu season.

Q4. I want [Specified child] to be vaccinated for flu next year

	%
Strongly agree	59
Agree	34
Neither agree nor disagree	5
Disagree	1
Strongly disagree	2

Q5. I intend [Specified child] to be vaccinated for flu next year

	%
Strongly agree	57
Agree	36
Neither agree nor disagree	6
Disagree	1
Strongly disagree	2

Q6. The healthcare worker vaccinating your child is a possible source of information about the child flu vaccine. Considering what you know, please select the number between the pair of words that best describes your feelings about information from the healthcare worker vaccinating your child.

	1 %	2 %	3 %	4 %	5 %	
Can't be trusted	2	1	9	25	64	Can be trusted
Is inaccurate	2	1	10	33	54	Is accurate
Is unfair	3	2	13	29	54	Is fair
Doesn't tell the whole story	4	3	19	34	42	Tells the whole story
Is biased	3	3	26	28	40	Is unbiased

Base: Can be trusted, n=194; is accurate, n=192; is fair, n=192; tells the whole story, n=193; is unbiased, n=192

Q7. These questions relate to your child's sensitivity to medicines. To what extent, if at all, do you agree or disagree with the following statement?

	[Specified child]'s body is very sensitive to medicines	[Specified child]'s body overreacts to medicines	[Specified child] usually has a stronger reaction to medicines than most other children I know	[Specified child] has had a bad reaction to medicines in the past	Even small amounts of medicine can upset [Specified child]'s body
	%	%	%	%	%
Strongly agree	2	1	0	1	0
Agree	6	1	2	5	1
Neutral	30	17	25	9	9
Disagree	36	49	46	46	49
Strongly disagree	26	34	36	40	41

Base: [Specified child]'s body is very sensitive to medicines, n=195; [Specified child]'s body overreacts to medicines, n=194; [Specified child] usually has a stronger reaction to medicines than most other children I know, n=195; [Specified child] has had a bad reaction to medicines in the past, n=195; Even small amounts of medicine can upset [Specified child]'s body, n=195

Appendix 13. Similarity ratings task

Man-made health threat items

1) Your travel vaccination

You went to the health centre to get a vaccination before travelling. The nurse used a needle to inject the vaccine into your arm. Surrounding the injection site, your arm turned red and was slightly *swollen (sw-ll-n)*

Did the doctor give you the travel vaccine? [no]

You had a normal reaction to the travel vaccine (T+)

You had an allergic reaction to the travel vaccine (T-)

You didn't have to wait at all for your travel vaccination (F+)

You had a long wait for your travel vaccination (F-)

2) Washing up liquid

You went to the supermarket to buy some washing up liquid, but the brand you usually buy was out of stock. You bought a different brand and went home, washed your dishes and prepared a large meal. When you finished eating you began to feel a pain in your *stomach (st-m-ch)*

Did you go to the corner shop to buy washing up liquid? [no]

You ate too much and are uncomfortably full (T+)

The new brand of washing up liquid has contaminated your plates making you feel ill (T-)

You enjoy keeping things clean (F+)

You dislike washing the dishes (F-)

3) Minor surgery

You were advised to have some minor surgery to correct a painful in-grown toenail. You were given an injection to help you relax and drift off to sleep. When you woke up, a doctor came over to tell you the outcome of your *procedure (pr-c-d-r-)*

Have you had minor surgery on your toe? [yes]

The surgery went well and you no longer have any pain (T+)

The surgery went badly and you still have considerable pain (T-)

You don't mind going to hospitals (F+)

You dislike going to hospitals (F-)

4) New Tablets

When you meet your friend for a drink they tell you that they have been feeling a bit under the weather. They explain that they went to the doctor and were given some new tablets that they have not taken before. After leaving your friend you think about whether the new tablets will help them feel better *(b-tt-r)*

Did you meet your friend for lunch? [no]

You expected the new tablets to soon make your friend feel better (T+)

You expected the new tablets might not work or could have unpleasant side effects (T-)

You get on well with your friend (F+)

You and your friend have a difficult relationship (F-)

5) Headache at work

You have an important meeting at work that needs to go well. About an hour before the meeting starts you find you have a splitting headache. You decide to take some *pain killers (p—n k-ll-rs)*

Did you have an important meeting at work? [yes]

The pain killers helped the meeting run smoothly (T+)

The pain killers were not effective and the meeting was difficult (T-)

You have an easy journey to work (F+)

You have a long and difficult journey to work (F-)

6) <u>A new mobile phone</u>

You recently bought a new mobile phone, which is equipped with lots of features, such as GPS, wi-fi and data roaming. While you sleep you put the phone next to your head on your bedside table. In the morning, you wake up with a *headache (h--d-ch-)*

Did you buy a new mobile phone recently? [yes]

You must have slept badly and after a while your headache disappears (T+)

Sleeping with your new mobile phone close to your head gave you a headache (T-)

You like the design of your new mobile phone (F+)

You dislike the design of your new mobile phone (F-)

7) <u>Mobile phone towers</u>

A new mobile phone tower has recently been constructed not far from your house. For the past few days you have been working in a new job and think it is

very demanding. On the way home from work you notice that you feel very *anxious (-nx---s)*

Have you been in your job for a long time? [no]

You have had a long day at work and when you relax at home you feel less anxious (T+)

The new mobile phone tower is making you feel anxious (T-)

The mobile phone tower blends in to the landscape (F+)

The mobile phone tower is ugly in the landscape (F-)

8) Moving to the city

You used to live in the countryside but were offered a job in a big city. After moving to the city you started taking the bus to work. Recently you have noticed that you become short of breath when taking the *stairs (st--rs)*

Do you live in a big city? [yes]

You get short of breath on the stairs now because you don't get as much exercise (T+)

You get short of breath on the stairs now because of the poorer air quality in the city (T-)

You like city living (F+)

You dislike city living (F-)

9) Hosting a dinner party

You hosted a dinner party for your friends and bought the ingredients from local farmers. When you bought the vegetables, the farmer told you he has been using a

new kind of pesticide. Your friends seemed to enjoy the meal but afterwards your tummy started *hurting (h-rt-ng)*

Did your colleagues come to the dinner party you were hosting? [no]

After the dinner party you relax and realise that you are just full (T+)

After the dinner party you think you feel sick because of the new pesticide that the farmer used on the vegetables (T-)

You like to try out new recipes at dinner parties (F+)

You do not usually try new recipes out at dinner parties (F-)

10) The factory

You have recently moved to a new flat on the top floor of a building that has no lift. There is a factory a few roads away which releases lots of fumes into the air. When you get home in the evenings after work you feel tired and out of *breath (br--th)*

Did you move house recently? [yes]

You are tired and out of breath from walking up the stairs to your new flat (T+)

The fumes from the factory are making you feel tired and out of breath (T-)

There is lots to do in your new area (F+)

There is not much to do in your new area (F-)

Naturally-occurring health threat items

1) Journey home

On your way home from work, you get on a crowded bus and have to stand very close to other people. The lady standing next to you starts to sneeze and cough. Later that evening you begin to feel a tickle in your *throat (thr--t)*

Were you sitting down on the bus? [no]

The feeling in your throat will go away once you've had a glass of water (T+)

The feeling in your throat is an indicator that you will develop an illness (T-)

You don't mind taking the bus even when it is very busy (F+)

You dislike taking the bus when it is very busy (F-)

2) Routine health check

You went to the clinic for your routine check. Your doctor asked you about your health in general and took your blood pressure. She looked at the pressure reading, and you saw her write down your *results (r-s-lts)*

Did the doctor take your temperature? [no]

Your blood pressure results were normal (T+)

Your blood pressure results were abnormal (T-)

You always go for your routine health check (F+)

You sometimes miss your routine health check (F-)

3) Headaches

You have had a few headaches recently. When you went to see your GP for a routine check, you decided to ask about them. The doctor examined you carefully and then told you his *findings (f-nd-ngs)*

Did you go to the GP for a routine check? [yes]

The doctor did not find anything unusual and thinks the headaches will go away (T+)

The doctor found something unusual related to the headaches that you have been getting (T-)

You ask the doctor lots of questions at your routine check up (F+)

You don't ask many questions at your routine check up (F-)

4) Hearing

For the last few weeks you have noticed that your hearing seems worse than it was. You decided that you should have your ears examined. After a thorough check, the doctor explained to you your *condition* (c-nd-t--n)

Have you noticed that your hearing has got better over the few weeks? [no]

The doctor explains that your hearing will rapidly recover (T+)

The doctor explains that your hearing will rapidly deteriorate (T-)

You did not have to wait long to see the doctor (F+)

You had to wait a long time to see the doctor (F-)

5) Winter approaching

It is approaching winter and the days are getting colder and darker. You know it is the beginning of the flu season and have seen more people sneezing at work. Walking home from work, you felt a gust of cold wind and started to *sneeze*. (sn--z-)

It is the beginning of the flu season? [yes]

The rush of cold air made you sneeze (T+)

You have caught the flu (T-)

You don't mind the cold weather in the winter (F+)

You dislike the cold weather in the winter (F-)

6) Your partner's flu

You live with your partner who has the flu. After work one day, you came home and threw their tissues away and cleaned the surfaces. Later on that evening you started to feel dizzy (*d-zzy*)

Is your partner feeling well? [no]

You are tired from the day and will feel better in the morning (T+)

You have caught the flu from your partner (T-)

Flu can be stopped from spreading through good hygeine (F+)

Flu spreads very quickly (F-)

7) Meeting a friend

You arranged to meet a friend after dinner, but have come home late from work. You grab some food in a rush, but after eating it you realized that the worktop was still dirty from last night's meal. Later, when you are with your friend you develop a stomach ache *(-ch-)*

Did you go to meet your friend after dinner? [yes]

You had a stomach ache because you ate in a rush and by the end of the evening it has disappeared (T+)

There must have been bacteria from the leftover food on the worktop which has made you ill (T-)

You enjoyed your dinner (F+)

You did not enjoy your dinner (F-)

8) Visiting a new restaurant

Last night you went to a new restaurant in town with your friend. You ordered chicken for your main course and noticed that it was a little bit pink. The meal was very large and on your way home you started to feel a bit *sick (s-ck)*

Did you go to a restaurant that you had been to before? [no]

You had a big meal and were just feeling very full (T+)

The chicken was undercooked and made you feel ill (T-)

You liked the atmosphere in the new restaurant (F+)

You didn't like the atmosphere in the new restaurant (F-)

9) Beach holiday

You went on a beach holiday in the summer. It is was very hot and the sun was strong. You noticed that a large number of people there were sunbathing *(s-nb-th-ng)*

Did you go on a summer holiday this year? [yes]

You reflected on how a lot of people find sun bathing pleasant and perhaps beneficial (T+)

You reflected on how harmful sunbathing can be (T-)

The beach was very clean (F+)

The beach was not as clean as you'd hoped (F-)

10) The tummy bug

Recently, lots of people at your work have been off sick because of a tummy bug that was going round. So far you have not been affected. One day, after lunch you began to feel a bit *ill*. (-ll)

Have other people at your work had a tummy bug? [yes]

You ate too much at lunch and felt a bit full (T+)

You caught the tummy bug that is going around the office (T-)

You talk to lots of people at work and have many friends there (F+)

You don’t talk to many people at work and have few friends there (F-)

Appendix 14. Similarity ratings task methods and results

Method

Study materials

Similarity ratings task

Similarity ratings task items were developed for this study. Items were adapted from Hoppitt et al. (519) or developed from scratch (see Appendix 13 for full item list).

Participants completed twenty items, ten related to man-made health threats and ten related to naturally-occurring health threats. Man-made health threats included vaccines, household cleaning products, having an operation, medications, mobile phones, mobile phone towers, pesticides and fumes and air pollution. Naturally-occurring health threats included illness (including headaches, stomach ache, hearing ability, blood pressure), influenza, bacteria and getting a sun-tan.

First, participants read twenty short passages presented in a fixed-random order; each passage was presented under a separate heading. Passages had ambiguous outcomes and the last word of each passage was incomplete. Participants filled in the first of the missing letters from the incomplete word and then answered a binary comprehension question (yes, no) about the passage.

An example follows:

> Minor surgery
>
> You were advised to have some minor surgery to correct a painful in-grown toenail. You were given an injection to help you relax and drift off to sleep. When you woke up, a doctor came over to tell you the outcome of your *pr-c-d-r- (procedure)*
>
> Have you had minor surgery on your toe? [yes]

After having read all the passages, participants began the similarity ratings aspect of the task. Participants were shown the heading of each passage and four

statements which related to the passage in question. Two statements were the positive and negative interpretations of the ambiguous passage (target items). The other two statements did not relate directly to the passage, but were positive and negative interpretations of the situations in the passage (foil outcomes); these items control for response bias. Participants rated how similar the statements were to the passage on a four-point Likert scale from "very different" to "very similar." The statements for the example passage follow:

The surgery went well and you no longer have any pain (T+)

The surgery went badly and you still have considerable pain (T-)

You don't mind going to hospitals (F+)

You dislike going to hospitals (F-)

Bias scores were calculated for target and foil sentences separately by subtracting similarity ratings scores for negative statements (negative targets, T- and negative foils, F- respectively) from positive statements (positive targets, T+ and positive foils, F+ respectively). A positive score indicates a positive bias, while a negative score indicates negative bias.

Procedure

After having completed T2 materials, participants were asked if they wanted to complete an optional additional task: the similarity ratings task. Participants were also asked at the end of T3 if they wanted to complete the similarity ratings task. Only participants who completed T2 and T3 materials online were asked to complete the similarity ratings task.

Data analysis

To investigate whether there was an association between interpretation bias and vaccine behaviours, I conducted a series of mixed model, repeated measures ANOVAs. Between participant factors were side-effect perception at T2 and T3 (side-effect perception, no side-effect perception), re-vaccination intention (intend to vaccinate, do not definitely intend to vaccinate) and actual re-vaccination (vaccinated, not vaccinated). Within-participant factors were the

source of the health threat (man-made, naturally-occurring) and item type (target, foil).

Results

Participants

83 parents initiated similarity ratings task items. To be included in the analyses, participants must have completed at least six natural and six man-made items. Thus, similarity ratings task analyses are presented for 45 parents. Participant characteristics for the similarity ratings task are shown in Table 26.

Table 26. Parent and child personal and clinical characteristics for those included in similarity ratings task analyses and associations with perception of side-effects from vaccination, re-vaccination intention for 2017/18 and re-vaccination in 2017/18

Participant characteristics	Level	Side-effects reported at T2			Side-effects reported at T3			Re-vaccination intention for 2017/18 season			Re-vaccination in 2017/18 season		
		Side-effects perceived n=17, n (%)	No side-effects perceived n=25, n (%)	p	Side-effects perceived n=12, n (%)	No side-effects perceived n=24, n (%)	p	Do not intend to re-vaccinate n=3, n (%)	Intend to re-vaccinate n=42, n (%)	p	Not re-vaccinated n=7, n (%)	Re-vaccinated n=35, n (%)	p
Parent gender	Female	14 (40.0)	21 (60.0)	1.00	10 (34.5)	19 (65.5)	1.00	2 (5.3)	36 (94.7)	.41	6 (17.1)	29 (82.9)	1.00
	Male	3 (42.9)	4 (57.1)		2 (28.6)	5 (71.4)		1 (14.3)	6 (85.7)		1 (14.3)	6 (85.7)	
Parent age	35+	14 (42.4)	19 (57.6)	1.00	8 (30.8)	18 (69.2)	.39	3 (9.1)	30 (90.9)	1.00	4 (12.9)	27 (87.1)	1.00
	18-34	3 (37.5)	5 (62.5)		3 (50.0)	3 (50.0)		0 (0.0)	8 (100.0)		1 (12.5)	7 (87.5)	
Parent chronic illness	Present	4 (40.0)	6 (60.0)	1.00	3 (37.5)	5 (62.5)	1.00	1 (10.0)	9 (90.0)	1.00	2 (22.2)	7 (77.8)	.31
	None	13 (40.6)	19 (59.4)		8 (32.0)	17 (68.0)		2 (6.3)	30 (93.8)		3 (9.7)	28 (90.3)	
Other 'at risk' people in child's household	Yes	10 (50.0)	10 (50.0)	.34	6 (37.5)	10 (62.5)	1.00	1 (5.0)	19 (95.0)	1.00	1 (5.3)	18 (94.7)	.60
	No	7 (35.0)	13 (65.0)		5 (33.3)	10 (66.7)		1 (5.0)	19 (95.0)		3 (15.8)	16 (84.2)	
Child gender	Female	10 (40.0)	15 (60.0)	.94	6 (31.6)	13 (68.4)	.81	2 (7.7)	24 (92.3)	1.00	4 (16.7)	20 (83.3)	1.00
	Male	7 (41.2)	10 (58.8)		6 (35.3)	11 (64.7)		1 (5.3)	18 (94.7)		3 (16.7)	15 (83.3)	
First-born child	Yes	12 (52.2)	11 (47.8)	.12	8 (38.1)	13 (61.9)	.70	3 (13.0)	20 (87.0)	.24	2 (8.7)	21 (91.3)	.63
	No	5 (26.3)	14 (73.7)		3 (25.0)	9 (75.0)		0 (0.0)	19 (100.0)		3 (17.6)	14 (82.4)	
Child age	Range 2 to 4 years	N=17, M=3.12, SD=0.86	N=25, M=2.96, SD=0.74	.53	N=12, M=3.08, SD=0.90	N=24, M=2.96, SD=0.69	.65	N=3, M=3.33, SD=1.16	N=42, M=3.00, SD=0.77	.48	N=7, M=2.71, SD=0.76	N=35, M=3.03, SD=0.79	.34
Child chronic illness	Present	2 (66.7)	1 (33.3)	.56	1 (33.3)	2 (66.7)	1.00	0 (0.0)	3 (100.0)	1.00	0 (0.0)	3 (100.0)	1.00
	None	15 (38.5)	24 (61.5)		10 (33.3)	20 (66.7)		3 (7.7)	36 (92.3)		5 (13.5)	32 (86.5)	
Child up-to-date with other routine vaccines	Not fully UTD	0 (0.0)	1 (100.0)	1.00	0 (0.0)	0 (0.0)	†	0 (0.0)	1 (100.0)	1.00	0 (0.0)	0 (0.0)	†
	UTD	17 (41.5)	24 (58.5)		11 (33.3)	22 (66.7)		3 (7.3)	38 (92.7)		5 (12.5)	35 (87.5)	

* $p \leq .05$

Abbreviations: UTD = up-to-date

† Unable to run due to lack of numbers

Side-effect perception at T2

Of participants included in similarity ratings task analyses, seventeen reported side-effects three days after vaccination while twenty-five did not. No personal or clinical characteristics were found to differ by side-effect perception at T2. Table 27 shows mean bias scores by outcome.

There was a main effect of source of health threat ($F(1,40)= 7.49$, $p=.01$, $\eta_p^2=.16$; see Table 28) on bias with more negative bias for naturally-occurring health threats (M=-0.17, 95% CI [-0.24 to -0.09]) than man-made health threats (M=-0.05, 95% CI [-0.14 to 0.03]). There was also a main effect of item type ($F(1,40)= 39.67$, $p<.001$, $\eta_p^2=.50$), with more negative bias for target items (M=-0.34, 95% CI [-0.46 to -0.21]) compared to foil items (M=0.12, 95% CI [0.05 to 0.19). There was an interaction seen between source of health threat and item type ($F(1,40)= 6.46$, $p=.02$, $\eta_p^2=.14$), with a difference between bias for man-made and naturally-occurring health threats only in the target item condition (target items: $t(41)=3.03$, $p=.004$; foil items $t(41)=0.18$, $p=.86$; see Figure 11). There was no main effect of side-effect perception at T2 on negative interpretation bias ($F(1,40)= 0.46$, $p=.83$, $\eta_p^2=.001$), nor were there any other interaction effects.

Table 27. Mean interpretation bias scores (95% CI) by perception of side-effects from vaccination, re-vaccination intention for 2017/18 and re-vaccination in 2017/18

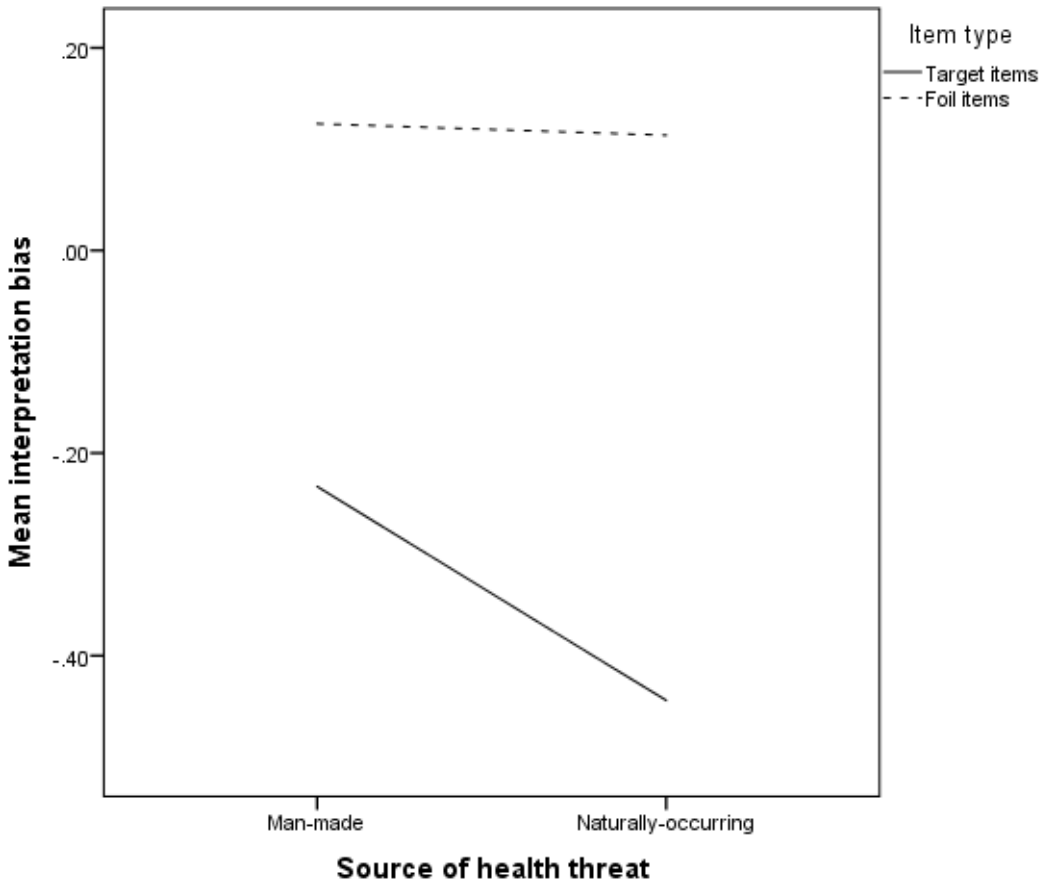
	Perception of side-effects at T2		**Perception of side-effects at T3**		**Re-vaccination intention in 2017/18 season**		**Re-vaccination in 2017/18 season**	
	Side-effects perceived n=17	**No side-effects perceived n=25**	**Side-effects perceived n=12**	**No side-effects perceived n=24**	**Do not intend to vaccinate n=3**	**Intend to vaccinate n=42**	**Not re-vaccinated n=7**	**Re-vaccinated n=35**
Man-made health threat target items	-0.25 (-0.45 to -0.05)	-0.22 (-0.44 to 0.004)	-0.06 (-0.36 to 0.25)	-0.27 (-0.48 to -0.05)	0.04 (-1.58 to 1.65)	-0.24 (-0.38 to -0.09)	-0.33 (-0.74 to 0.07)	-0.20 (-0.37 to -0.03)
Man-made health threat foil items	0.16 (-0.02 to 0.29)	0.09 (-0.004 to 0.19)	0.15 (0.003 to 0.29)	0.13 (-0.01 to 0.26)	-0.04 (-0.20 to 0.122)	0.15 (0.06 to 0.25)	0.03 (-0.07 to 0.13)	0.12 (0.04 to 0.21)
Naturally-occurring health threat target items	-.05 (-0.73 to -0.27)	-0.39 (-0.55 to -0.23)	-0.36 (-0.64 to -0.08)	-0.41 (-0.59 to -0.24)	-0.47 (-1.83 to 0.89)	-0.41 (-0.54 to -0.28)	-0.40 (-0.87 to 0.07)	-0.42 (-0.56 to -0.28)
Naturally-occurring health threat foil items	0.12 (0.03 to 0.22)	0.10 (-0.02 to 0.23)	0.17 (0.01 to 0.32)	0.15 (-0.004 to 0.30)	-0.03 (-0.18 to 0.11)	0.15 (0.05 to 0.24)	-0.01 (-0.23 to 0.20)	0.13 (0.04 to 0.22)

Table 28. Results of three-way ANOVAs between interpretation bias and perception of side-effects from vaccination, re-vaccination intention for 2017/18, re-vaccination in 2017/18

		F (df)	p	Partial eta squared
Side-effect perception at T2	Source of health threat (man-made, naturally-occurring)	7.4 (1,40)	.01*	.16
	Side-effect perception (side-effect perceived, no side-effects perceived)	0.05 (1,40)	.83	.001
	Item type (target, foil)	39.67 (1,40)	<.001*	.50
	Source of health threat*side-effect perception	0.59 (1,40)	.45	.02
	Item type*side-effect perception	0.60 (1,40)	.44	.02
	Source of health threat*item type	6.46 (1,40)	.02*	.14
	Source of health threat*side-effect perception*item type	0.06 (1,40)	.82	.001
Side-effect perception at T3	Source of health threat (man-made, naturally-occurring)	5.21 (1,34)	.03*	.13
	Side-effect perception (side-effect perceived, no side-effects perceived)	0.71 (1,34)	.40	.02
	Item type (target, foil)	24.59 (1,34)	<.001*	.42
	Source of health threat*side-effect perception	0.87 (1,34)	.36	.03
	Item type*side-effect perception	0.45 (1,34)	.51	.01
	Source of health threat*item type	7.23 (1,34)	.01*	.18
	Source of health threat*side-effect perception*item type	0.69 (1,34)	.41	.02
Re-vaccination intention for 2017/18	Source of health threat (man-made, naturally-occurring)	5.12 (1,43)	.03*	.11
	Re-vaccination intention (intend to re-vaccinate, do not intend to re-vaccinate)	0.07 (1,43)	.79	.002
	Item type (target, foil)	5.68 (1,43)	.02*	.12
	Source of health threat*intend to re-vaccinate	1.18 (1,43)	.28	.03
	Item type* intend to re-vaccinate	1.13 (1,43)	.29	.03
	Source of health threat*item type	5.60 (1,43)	.02*	.12
	Source of health threat* intend to re-vaccinate *item type	1.46 (1,43)	.23	.03
Re-vaccination in 2017/18	Source of health threat (man-made, naturally-occurring)	2.29 (1,40)	.14	.05
	Vaccinated (re-vaccinated, not re-vaccinated)	0.94 (1,40)	.34	.02
	Item type (target, foil)	17.91 (1,40)	<.001*	.31
	Source of health threat*re-vaccinated	0.23 (1,40)	.64	.01
	Item type*re-vaccinated	0.11 (1,40)	.74	.003
	Source of health threat*item type	1.55 (1,40)	.22	.04
	Source of health threat*re-vaccinated*item type	1.09 (1,40)	.30	.03

*$p \leq .05$

Figure 11. Mean negative interpretation bias by source of health threat, item type and side-effect perception at T2



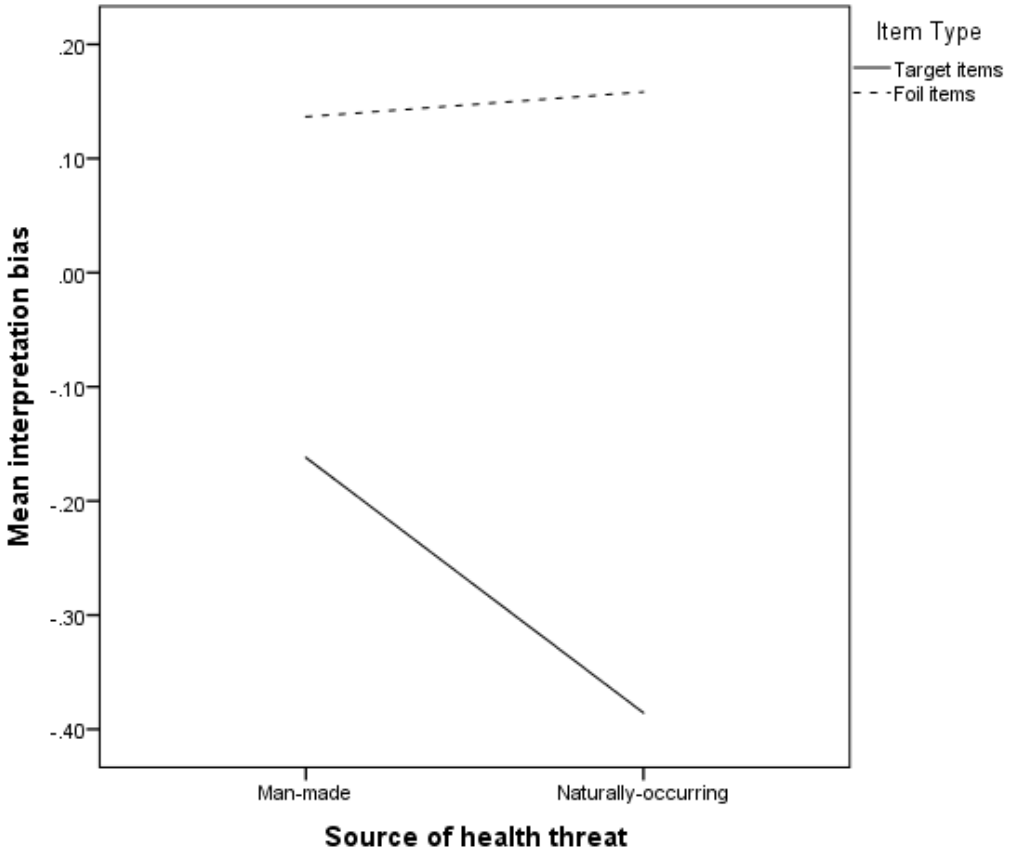
Side-effect perception at T3

Of participants included in similarity ratings task analyses, twelve reported side-effects one month after vaccination while twenty-four did not. No personal or clinical characteristics were found to differ by side-effect perception at T3.

There was a main effect of source of health threat ($F(1,34)= 5.21$, $p=.03$, $\eta_p^2=.13$; see Table 28) on bias with more negative bias for naturally-occurring health threats (M=-0.11, 95% CI [-0.21 to -0.01]) than man-made health threats (M=-0.01, 95% CI [-0.12 to 0.09]). There was also a main effect of item type ($F(1,34)= 24.59$, $p<.001$, $\eta_p^2=.42$), with more negative bias for target items (M=-0.27, 95% CI [-0.42 to -0.13]) compared to foil items (M=0.15, 95% CI [0.04 to 0.25). There was an interaction seen between source of health threat and item type ($F(1,40)= 6.46$, $p=.02$, $\eta_p^2=.14$), with a difference between means for man-made and natural health sources only in the target item condition (target items: $t(35)=2.64$, $p=.01$;

foil items $t(35)=-0.58$, $p=.57$; see Figure 12). There was no main effect of side-effect perception at T3 ($F(1,34)= 0.71$, $p=.40$, $\eta_p^2=.02$) on negative interpretation bias, nor were there any other interaction effects.

Figure 12. Mean negative interpretation bias by source of health threat, item type and side-effect perception at T3



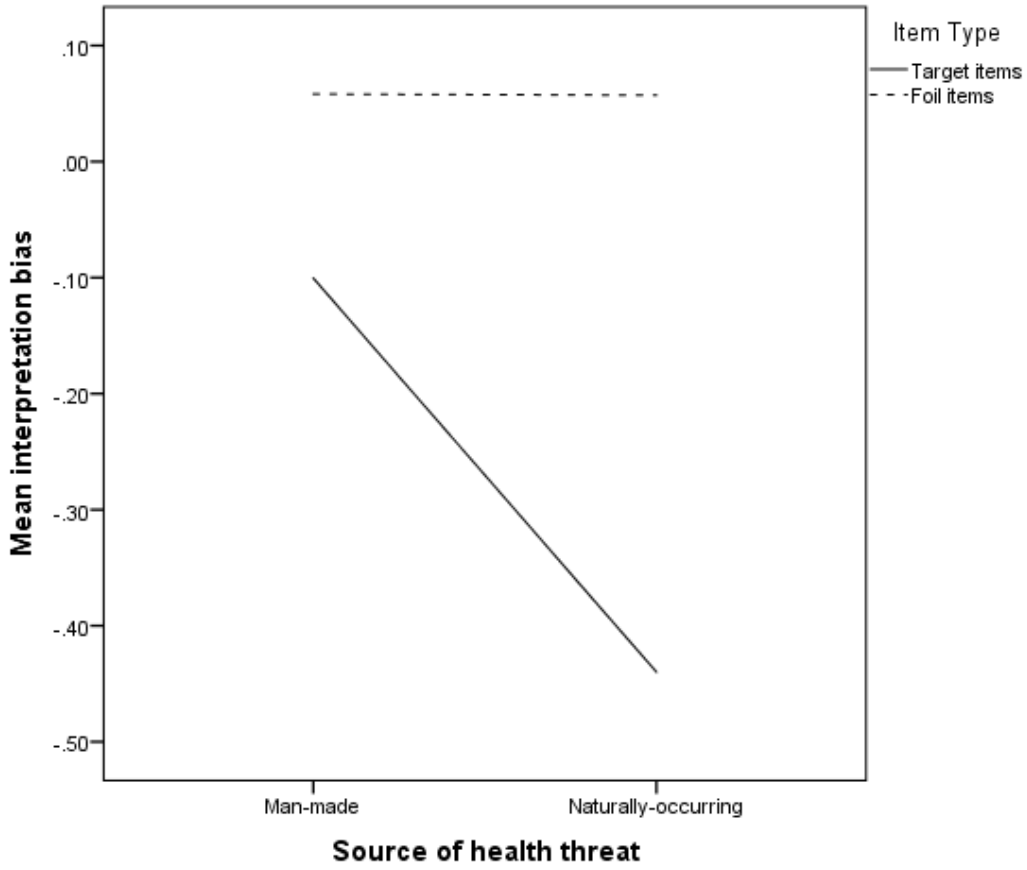
Re-vaccination intention for 2017/18

Of participants included in similarity ratings task analyses, 42 intended to re-vaccinate their child in 2017/18 while three did not definitely intend to re-vaccinate their child. No personal or clinical characteristics were found to differ by re-vaccination intention.

There was a main effect of source of health threat ($F(1,43)= 5.12$, $p=.03$, $\eta_p^2=.11$; see Table 28) on bias with more negative bias for naturally-occurring health threats (M=-0.19, 95% CI [-0.35 to -0.03]) than man-made health threats (M=-0.02, 95% CI [-0.19 to 0.15]). There was also a main effect of item type ($F(1,43)= 5.68$, $p=.02$, $\eta_p^2=.12$), with more negative bias for target items (M=-0.27, 95% CI

[-0.51 to -0.03]) compared to foil items (M=0.06, 95% CI [-0.10 to 0.22). There was an interaction seen between source of health threat and item type (F(1,40)= 6.46, p=.02, η_p^2=.14), with a difference between means for man-made and natural health sources only in the target item condition (target items: t(44)=3.05, p=.004; foil items t(44)=0.14, p=.89; see Figure 13). There was no main effect of intention on negative interpretation bias (F(1,43)= 0.07, p=.79, η_p^2=.002), nor were there any other interaction effects.

Figure 13. Mean negative interpretation bias by source of health threat, item type and re-vaccination intention for 2017/18



Re-vaccination in 2017/18

Of participants included in similarity ratings task analyses, thirty-five re-vaccinated their child in the 2017/18 influenza season while seven did not. No personal or clinical characteristics were found to differ by re-vaccination in 2017/18.

There was a main effect of item type ($F(1,40)= 17.91$, $p<.001$, $\eta_p^2=.31$), with more negative bias for target items (M=-0.34, 95% CI [-0.51 to -0.17]) compared to foil items (M=0.068, 95% CI [-0.02 to 0.16). There was no main effect of re-vaccination or source of health threat on negative interpretation bias ($F(1,40)= 0.94$, $p=.34$, $\eta_p^2=.02$), nor were there any interaction effects.

Appendix 15. Personal and clinical characteristics of those who were and were not included in interpretation bias analyses in the prospective cohort study

	Level	Included in analyses (n=75), n (%)	Not included in analyses (n=121), n (%)	p
Parent gender	Female	58 (35.2)	107 (64.8)	.04*
	Male	17 (54.8)	14 (45.2)	
Parent age	35+	48 (40.7)	70 (59.3)	.25
	18-34	27 (50.0)	27 (50.0)	
Parent chronic illness	Present	20 (40.8)	29 (59.2)	.70
	None	55 (37.7)	91 (62.3)	
Other 'at risk' people in child's household	Yes	29 (40.3)	43 (59.7)	.67
	No	39 (37.1)	66 (62.9)	
Child gender	Female	40 (39.2)	62 (60.8)	.70
	Male	34 (36.6)	59 (63.4)	
First-born child	Yes	48 (39.7)	73 (60.3)	.61
	No	27 (36.0)	48 (64.0)	
Child age	2-4 years	N=74, M=2.96, SD=0.94	N=120, M=3.20, SD=-.89	.08
Child chronic illness	Present	6 (33.3)	12 (66.7)	.65
	None	69 (38.8)	109 (61.2)	

*$p \leq .05$